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COVID-19: THREE PHASES OF THE PANDEMIC
Dynamics of cases, deaths and tests related to SARS-CoV-2
A systematic analysis of 213 countries and territories

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Mary Jo Takach, No Cure for that Cold?
"The common cold is like the weather – everybody talks about it but no one can do much about it ... A new group of viruses has also been isolated. These are called 'human coronaviruses' and they also cause typical colds... Dr. James Spray estimates that there are at least 200 cold viruses ... The U.S. National Institutes of Health (NIH) closed down its Board of Vaccine Development last year, deciding it was a waste of time and money". [This World (San Francisco, CA), 1972, Oct 8, Sun, N 41: 28].

Abstract

Background

Since the previous study dealing with the case fatality ratio and infection fatality ratio caused by COVID-19, the author has received many comments that prompted the question: "Why did an optimistic prognosis fail?" To answer this question, a more detailed and expanded analysis was carried out in a new study.

Objective

To evaluate the dynamics of monthly numbers of cases, deaths, tests and CFR worldwide during three phases of the COVID-19 pandemic.

Material and Methods

Twenty three sets of databases, dated the 22nd of each month from January 2020 to November 2021, for 213 countries were collected from the Worldometer website. The number of cases, deaths, tests, CFR, IFR, etc. were counted for various periods of time for each of the 213 countries, then results related to different periods of time were compared.

Results

The analysis of the main epidemiological parameters led to the division of three phases of the global pandemic evolution. The first phase (23.01.20-22.07.20), the second phase (23.07.20-22.01.21) and the third phase (23.01.21-22.07.21) were different in terms of the number of tests performed, new cases, and mortality due to COVID-19. By the end of the second phase, the worldwide statistics indicated the imminent end of the pandemic, but the third phase was characterized by a sudden rise in the number of new cases and deaths that could not be explained rationally. The most dramatic evolution of the epidemic curve occurred in the countries where doctors had successfully battled COVID-19 during the first two phases of the pandemic.

Conclusions

Despite the decrease in overall death numbers during the latest months analyzed, additional study is necessary to identify the cause for the increase in the number of new cases and deaths during the third phase of the pandemic.

Only complete information regarding the positive and negative impact of medical and non-medical methods of diagnostics and prophylaxis of COVID-19 can help to organize effective measures to end the current pandemic and prevent a similar one from occurring in the future.

Presumably, there are several causes of the negative evolution of the current pandemic, including the overreliance on PCR tests, application of non-specialized premises for quarantine and treatment, decrease in herd and individual immunity, inadequate change of therapeutic protocols, and ignoring prophylactic treatment.

It can be suggested that the use of immunemodulatory drugs, for example, thymus extract or thymic peptides, in groups of people with compromised immunity is necessary, and prophylactic and therapeutic protocols should be changed from the 'standard' types to 'personalized' ones.

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Background

Since the previous study dealing with the case fatality ratio and infection fatality ratio caused by COVID-19,[1] the author has received many comments that prompted the question: "Why did an optimistic prognosis fail?" To answer this question, a more detailed and expanded analysis was carried out in a new study.

1. Introduction

1.1. Initial and current state of the COVID-19 pandemic narrative

On December 31, 2019, the WHO's China Country Office was alerted to cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province of China.[2] On January 3, 2020, the first complete genome of the novel coronavirus (2019-nCoVs) was identified.[3] On February 11, 2020, a new disease was named "the coronavirus disease 2019" or CoViD-19.[4] Further studies revealed that SARS-CoV-2 was circulating in various countries, including Spain,[5] Italy,[6] India,[7] France,[8] USA,[9] etc. before the outbreak of the epidemic in China.[10-11]

During the initial stage of the COVID-19 pandemic two well-known discoveries, namely: "Unique inserts in the 2019-nCoV spike protein" and "Reduction and functional exhaustion of T-Cells" in COVID-19 patients,[12-13] were published. These discoveries demonstrated structural and functional similarities between two viruses and prompted a common sense question about the origin of SARS-CoV-2.[14-15] Questions about the origins of the virus resurfaced in December 2020 when production of an Australian vaccine was discontinued as healthy vaccinated people became tested positive for HIV.[16]

Other issues related to the epidemic curve that had anomalous evolution include:

(1) *New patterns*:

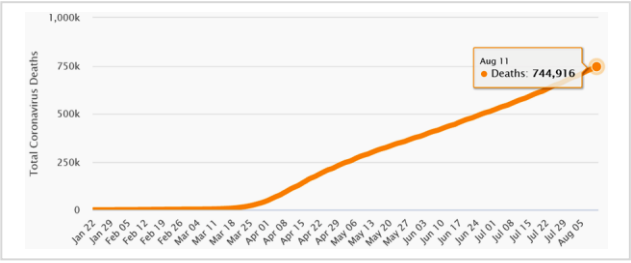
In April 2020, an expert in epidemiology, Prof. Vladimir Nikiforov mentioned: "if the virus followed the 'classical pattern', the epidemic would have ended within three months, but now we are faced with something new".[17]

(2) *Data adjustments*:

During the first half of the pandemic there were many cases of local number adjustments that affected the worldwide statistics related to COVID-19.[18] (Fig. 1)

On April 26, 2020, a cumulative report of Palestine was reduced by 153 cases; on May 25, 2020, a report of Spain was reduced by 1915 deaths; on June 3, 2020, a report of France was reduced by 37,895 cases; on June 20, 2020, a report of Mayotte was reduced by 787 cases; on August 13, 2020, a report of the United Kingdom was reduced by 29,726 cases and by 5,319 deaths.[18] (Fig. 2)

(a)



(b)

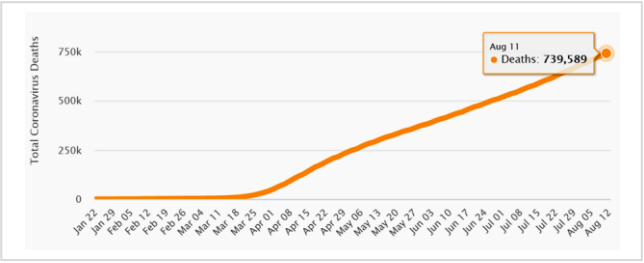


Figure 1. Worldometer: Adjustment of the worldwide cumulative number of deaths.[18]
These are two screenshots dated (a) August 12, 2020, 07:27 GMT; and (b) August 13, 2020, 09:18 GMT.
The total number of deaths decreased suddenly from 744,916 to 739,589 cases.

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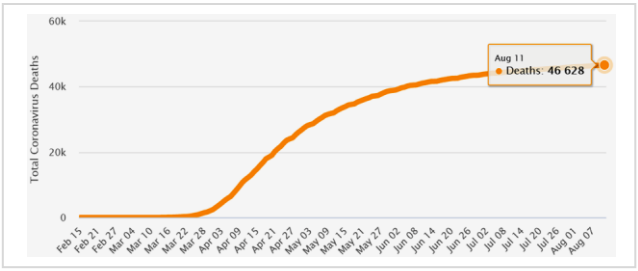
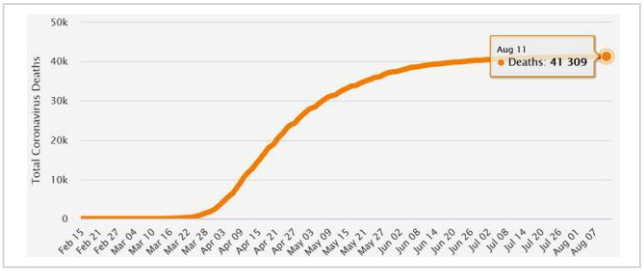
(a)

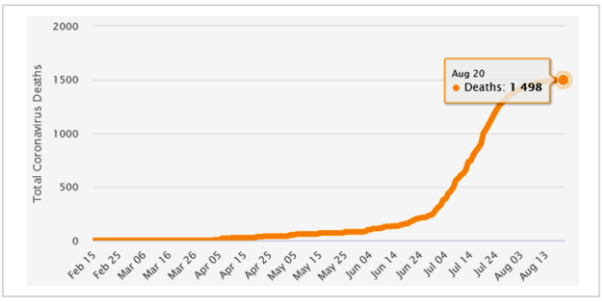


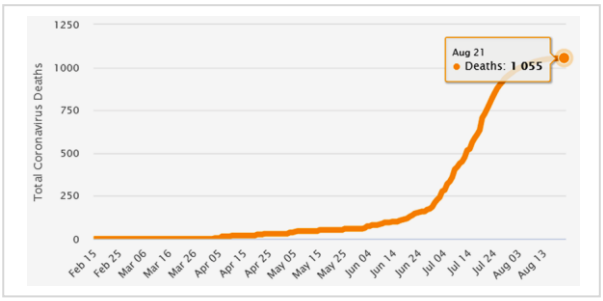


(b)

Figure 2. Worldometer: Adjustment of cumulative number of deaths in the United Kingdom.[18]
These are two screenshots dated (a) August 12, 2020, 07:34 GMT; and (b) August 13, 2020, 08:19 GMT.

(a)





(b)

Figure 3. Worldometer: Adjustment of cumulative number of deaths in Kyrgyzstan.
These are two screenshots dated (a) August 21, 2020, 08:21; and (b) August 22, 2020, 08:04 GMT.[18]

On August 14, 2020, a report of Peru increased by 3,935 new deaths; on August 21, 2020, the number of deaths in Kyrgyzstan, decreased by 443 cases (Fig. 3); on September 24, 2020, a record of Liberia, decreased by 133 cases,[18] etc. Similar adjustments took place during the later period of the pandemic: on July 2, 2021, it was reported, "Santa Clara County's COVID-19 death toll drops by 505",[20] and so on.

(3) *A synchronization-like phenomena*:

The first example of synchronization was a weekly mortality cycle which was noticed in June 2020,[21] later this anomalous cycle of daily death became obvious and steady.[22] A comparison of the percentage of fatal cases on different days of the week for a period of 100 weeks (26.01.20-25.12.21) revealed almost identical distribution as described in a previous study.[22] (Fig. 4).

There is another example of synchronization related to the daily new cases of COVID-19. During 1.5 years of the pandemic the highest number of daily new cases in the United States and the United Kingdom were recorded on the same day, on January 8, 2021; together they accounted for 44% of the total number of new cases worldwide.[18]

(4) *A Strange evolution of the pandemic*:

In mid December 2021, a well-known expert in infectious diseases, Dr. Anthony Fauci, said: "it's 'unprecedented' how long

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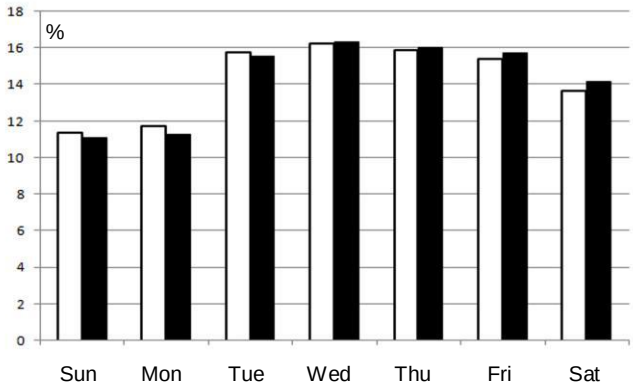

Figure 4. Global mortality due to COVID-19 on various days of the week: white columns - period of 100 weeks (26.01.20-25.12.21); black columns – period of 40 weeks (01.03.20-05.12.20). The vertical axis shows percentages; the horizontal axis shows days of the week.

the COVID-19 pandemic has lasted globally, with many countries enduring multiple major waves of infections since it was declared in March 2020".[23] So, a pertinent question that pops up is: why, despite unprecedented control measures to prevent the spread of a new virus, including worldwide quarantines, isolation, movement control order, curfew, social distancing, wearing of masks and mass vaccinations, the epidemic curve still has a 'wave-like' or 'propagated' shape instead of going down? Were preventive measures effective, or simply useless or harmful?

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1.2. Infectious disease – a battle between the human body's defense and viruses or bacteria

History of the battle against viruses and bacteria goes back at least several thousand years. Ancient physicians already knew about external pathogens which could cause acute febrile diseases. They also knew that an evolution of any clinical case depended on the health status of the patient before the onset of the disease, so they talked about "body defense".[24] At the beginning of modern microbiology the importance of body resistance was confirmed by a Prof. Max von Pettenkofer, who swallowed the entire contents of a tube filled with germs of cholera, but nothing happened to him. So he claimed: "The important thing is the *disposition* of the individual!"[25]

Despite a variety of external pathogens, the human body has a limited number of defense mechanisms, which is accompanied by a few clinical syndromes, consisting of common symptoms, such as fatigue, chills or hot feeling, headache, cough, shortness of breath, nausea, vomiting, diarrhea, skin rashes or discoloration of the skin, etc.

In ancient times the mechanism of the onset of fever was differentiated into two main groups based on the presence of thirst, sweating, chills, or feelings of heat; and the choice of individual treatment was determined by the type of fever. According to the modern view on fever, which commonly accompanies infectious diseases, one can define only two mechanisms leading to an increase in temperature: one is an increase in heat production and another, a decrease in heat transfer, or their combination.[26] Thus ancient and modern explanations of fever are quite similar, and two types of antipyretic medicines are necessary and sufficient to manage any case of excessive fever. Similarly, 2-3 mechanisms can be identified that underlie each of the remaining symptoms of any acute viral disease, so, a small group of commonly used drugs would be sufficient to manage any infectious diseases, including *old* and *new* ones.

After the discovery of bacteria and viruses as a cause of infectious diseases the main emphasis was changed from supporting the body resistance to the fighting against pathogens. It was successful in the majority of bacterial infection cases, but it was almost useless when disease was caused by a virus.

Therefore, if there is no etiotropic treatment, then there is no need to identify a *new* viral disease. All pharmaceutical and non-pharmaceutical therapeutic modalities would be addressed to the well-known protective mechanisms of the human body, and treatment should be based on the leading syndromes and symptoms, using the principle called *off label* therapy.

1.3. The classical foundation of medicine is wisdom, which is evergreen

Multiplication tables, the Pythogorean theorem, Archimedes' law, ideas of inertia and atomic structure of matter appeared several thousand years ago. In the course of history ancient knowledge developed and improved until it turned into higher Mathematics and quantum Physics, however, the multiplication table, Archimedes' law and other basic knowledge have not lost their value in our time.

Similarly, ancient medicine also had its own canon, preserved within the framework of traditional Chinese medicine. The most important law of that canon was postulate: to strengthen or reinforce that which is *deficient*, and drain or sedate that which is *excessive*.[27] Over the centuries, it has taken on new forms, and was introduced in the theory of *asthenic* and *sthenic* diseases by Dr. John Brown.[28] At the beginning of the 20th century, two physiologists presented this postulate in the form of theories of *parabiosis*[29] and *dominant*.[30] In the 1930s, Hans Selye discovered a dynamic interaction between excess and deficiency, and described General Adaptation Syndrome theory, which distinguished the *alarm phase* (= excess, sthenic disease, dominant) and *exhaustion phase* (= deficiency, asthenic disease, parabiosis).[31-32]

At the beginning of organotherapy[33-34] doctors used extracts of animal organs to treat various age-related problems, nowadays called *frailty*.[35-36] Later a modern branch of organotherapy, taking the form of hormonotherapy, became a powerful tool to treat various diseases caused by hormonal insufficiency.[37-38] They followed the first part of the ancient postulate: *to strengthen or reinforce that which is deficient*. When antibiotics were discovered, physicians got a tool to inhibit bacterial growth.[39] Application of antibiotics was an example of following the second ancient postulate: *drain or sedate that which is excessive*. But further development of medicine did not follow the basic canon.

Nowadays despite the fact that *deficiency* patterns are the causes of the majority of chronic diseases, especially among elderly people, antagonists, blockers, or inhibitors, such as α-blockers, β-blockers, calcium channel blockers, ACE inhibitors, PDF-5 inhibitors, and H2 antagonists are used for therapy. Before prescribing sedative therapy patients are not tested whether the corresponding target is in an excited state or not. So, a rational medical sense is ignored and patients have to take medication for all their life.

The same problem has arisen with the treatment of COVID-19. The main pathologic target was T-cell immune-deficiency,[13,40-41] nevertheless a lot of attention was paid to the cytokine storm which was a consequence, but not a primary cause. According to basic medical law, treatment should be focused more at restoring T-cell immunity,[42] and less against increased activity of certain components of the immune system.

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1.4. Treatment of patients suffering from acute infectious diseases

About 1800 years ago, Dr. Zhang Zhongjing summarized the results of research from previous generations and developed a theory of acute infectious diseases, which explained therapy based on leading clinical symptoms and syndromes.[43] According to this theory, there could be only 6 phases, and certain phases could have 2-3 variants. Thus, the whole variety of clinical syndromes related to infectious diseases was limited to 10-12 variants, each having specific treatment and prevention. (Fig. 5.b)

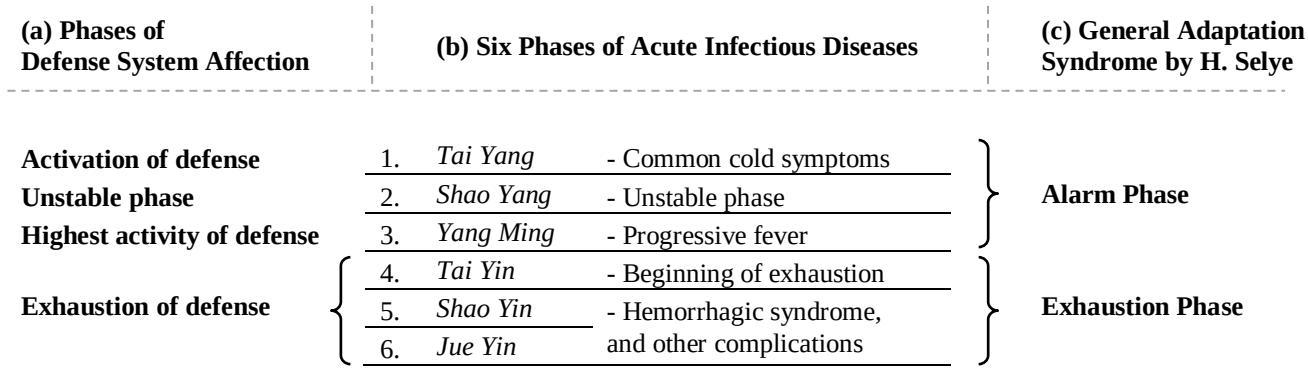

Figure 5. A comparison between various theories which describe phase evolution of acute infectious diseases:
(a) Four phases of diseases caused by external physical or biological pathogens called "excessive heat".[44]
(b) Six phases of diseases caused by various external physical, chemical or biological pathogens.[43]
(c) Two phases of diseases according to the general adaptation syndrome discovered by Hans Selye.[31-32,45]

There are some examples of treatment of the initial phases of infectious diseases: in the case of initial fever with general cold feelings without sweating – *Herba Ephedrae* was recommended; if there is initial fever with general hot feelings – *Folium Mori Albae* or *Herba Menthae Haplocalycis* should be used; if there is initial fever with intensive sweating or tension in the muscles – *Ramulus Cinnamomi Cassiae* was recommended; in the case of fever with alternating cold and hot feelings – *Radix Bupleuri*, was used, etc.[43] (Fig. 5.b). A change in symptoms pointed to a change in the phase of the disease and required an adjustment of therapy. If a patient has a severe fever with hemorrhagic symptoms, skin rashes, kidney and liver impairment, delirium, etc. – *Radix of Isatis tinctoria* should be applied.[44,46] (Fig. 5.a)

It would be useful for modern pathophysiology to distinguish between various types of the fever and choose antipyretic medicines (paracetamol, ibuprofen, etc) based on the pharmacodynamic of these popular drugs, but not empirically, as they are usually used.[47]

During later centuries, protocols of infectious disease treatment were updated according to the new scientific discoveries of that time. Excepting deadly epidemic diseases (plague, smallpox, or cholera), therapy of other infectious diseases was effective and successful. Theoretically, modern medicine having a long history in the past and advanced pharmaceutical science nowadays must be able to treat any problem more effectively than our predecessors, but the helplessness of the modern medical system during the current pandemic was beyond common sense,[48] and raised a question about the quality of medical education of the distinguished leaders and their followers.

1.5. Treatment of COVID-19 at initial phase of pandemic

At the beginning of the pandemic, WHO encouraged doctors to use well-known medicines as *off-label* treatment of a new disease since there were no approved drugs yet for the treatment of COVID-19.[49] The majority of knowledgeable and experienced doctors who received high quality medical education treated patients suffering from COVID-19 with great success. They recommended using anticoagulants, such as dipyridamole[50] or heparine;[51] antiviral and anti-inflammatory drugs, including ivermectin,[52-53] colchicine,[54-55] methylene blue,[56-57] chloroquine and hydroxychloroquine;[58-60] immune-modulators, such as thymic extracts,[61] thymic peptides,[62] solution of Formaldehyde,[63] melatonin[64] and common adjuvants.[65] A group of physicians, who had identified the similarity between COVID-19 and toxic damage to red blood cells, recommended to use therapeutic protocol which was effective in cases of acute intoxication.[66] Other experts recommended an inhalation with ethanol vapor[67-68] and helium-oxygen mixture,[69] since those methods had already been applied to similar cases before.[70-72] Plant derived medicines, including extracts of Artemisia, Isatis or Colchicum as well as green and black tea, and various complex prescriptions were also used either for prophylaxis or for combined therapy.[73-78]

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During the early days of the COVID-19 epidemic, doctors in Russia used their own treatment protocols, that resulted in very low mortality, and even raised questions and skepticism from the international medical community.[79-80] For example, in April-June 2020, in a hospital attached to the Moscow State University, 420 out of 424 indoor patients suffering from COVID-19 were successfully treated with routine medication. Effectiveness of the therapy was around 100%.[81]

As basic medicines these doctors used Colchicine, Dipyridamole, Bromhexine, and Spironolactone; additional application of certain anticoagulants and corticosteroids depended on a particular case.[82] Thus, common medical knowledge and experience were enough to treat the infectious disease caused by the *new* virus.

Every doctor knows that effective therapy of any patient requires individual approach due to the natural difference between even two *similar* cases, especially if a patient suffers from COVID-19.[83] Following standard protocols without dose adjustment and individual correction of used medicines in certain clinical trials resulted in decreasing or even losing effectiveness of the drugs that had been used by other doctors earlier on.[84] Nevertheless knowledgeable doctors continued their successful and effective treatment.[65,85-86] The therapeutic effects of the medicines mentioned above have been proven in further clinical trials and the results were published in peer-reviewed journals.[87]

After recent discussions on therapeutic protocols taking place between various experts, Dr. Peter A. McCullough recommended to his colleagues to treat COVID-19 patients according to their own knowledge and experience.[88] One can only deduce there is no common sense for doctors to follow the protocol of an expert or a country where mortality was high, otherwise they will gain the same high mortality among their patients.

1.6. Clinical trials

Early in the 18th century, homeopathic doctors, who studied *pathogenesis* of new remedies, introduced extensive and multi-centered clinical trials to the medical public. They needed to differentiate the primary and secondary symptoms, and to separate important symptoms from non-important ones, and so on. According to the demand of homeopathic pharmacy, there was a rationale for using large groups of people. Nevertheless extensive trials were criticized by Dr. Rudolf Virchow, the father of modern Pathology. He insisted that despite certain similarities in pathology discovered in different patients with a similar disease, each patient has his/her individual disease, so instead of using statistics collected from large groups of patients, doctors should pay more attention to detailed analysis of every particular case.[89]

As far as acute infectious diseases are concerned, their pathological condition is not stable, but has several phases. Each of the phases requires the use of different medicines and patient care. It would be illogical to look for the treatment of COVID-19 in general, but each phase of the disease requires an appropriate group of medicines. Then a doctor should choose one or two medicines taking into account the main symptoms of a certain patient. Multiple attempts to find a unique medicine against 'COVID-19' have failed. That means treatment of COVID-19 or any further new acute viral infectious diseases should be managed by means of routine drugs applied as *off label* therapy.

When COVID-19 was announced as a new disease,[4] healthcare worldwide was challenged to conduct new clinical trials to find medicines that were safe and effective in treating COVID-19 and comorbidities. After Dr. T. A. Ghebreyesus expressed an opinion about the pandemic,[48] all patients suspected of being infected with SARS-CoV-2 were automatically made participants of clinical trials which were the most extensive in the history of mankind.

Since all the pathogenic mechanisms encountered in COVID-19 were already well-known before April-May, 2020, the treatment of COVID-19 should not have been difficult.

Moreover, since some routine medicines had already been used successfully, the main goal of further clinical trials was to design the most effective and adjustable protocols, but not to reject the effects of the used medicines. That is why it is crucial that ongoing clinical trials should focus more on adjusting protocols to enhance the efficacy of the tested medicines, rather than adhering to some standard approach. Adhering to such rigid protocols might render the treatment of COVID-19 ineffective, not due to the ineffectiveness of the medicine per se but due to the inappropriate protocols applied. The trials also tested the ability of doctors to form homogeneous groups, taking into account the leading pathogenic mechanisms, presented among the patients in the group of study and the main therapeutic action of the studied medicine. Unfortunately, many ongoing clinical trials have ended up demonstrating insufficient knowledge and experience of the physicians conducting the research.

For experienced physicians with a solid background, clinical trials were not necessary. Since they knew the pathogenesis of COVID-19 and pharmacodynamic of the medicines used, in their clinics efficacy of therapy must be around 100%.[65,82,85,86] But results of clinical trials were very important and useful for beginners, since standard protocols help them to reduce the number of adverse reactions of their treatment.

1.7. Paradoxes of Clinical trials

There were some facts that would be worth paying attention to, since they could indicate possible causes of high mortality at the initial phase of the COVID-19 pandemic.

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In January-April, 2020, mortality among CoViD-19 patients who were treated with invasive mechanical ventilation (IMV) was higher than 80%, including, 81%,[90] 88.1%,[91] 92%,[92] and even 97%.[93] According to a review by G. Bellani, et al. published in 2016, the highest mortality among the severest cases of patients with Acute Respiratory Distress Syndrome (ARDS) of various origin, who were treated with IMV, was around 50%.[94]

After comparing the results of IMV application among COVID-19 patients with the results presented in the review on IMV (2016), one may conclude that IMV had no therapeutic value among patients with ARDS caused by SARS-CoV-2. The lack of a therapeutic effect of IMV was explained by systemic endotheliitis and coagulopathy which led to micro and macro-thromboses in various organs including the lungs.[95] Nevertheless, IMV is still in use to treat COVID-19 patients with ARDS.

From the outset of the COVID-19 pandemic, it was known that there would be a high risk group, comprising mainly of aged people with compromised immunity and comorbidities. The main parameter that could point to the risk of severe cases was lymphopenia.[93] Prognostically unfavorable signs of COVID-19 were: a decrease in the number of lymphocytes in general, a decrease in sub-populations of T-lymphocytes (CD4+, CD8+) and, as a consequence, a dysfunction of B-lymphocytes and dys-regulation of their production of Ig-M and Ig-G. The number of T-lymphocytes, including CD4+ and CD8+, was especially reduced among patients requiring treatment in the intensive care unit.[13] The severity of the case and outcome of COVID-19 largely depended on a patient's age, that correlated with a decrease in T-cells, due to the thymus atrophy.[40,96] The risk of COVID-19 hospitalization rises exponentially with age, inversely proportional to T-cell production.[41] In COVID patients, thymus enlargement was frequent and associated with increased T-lymphocytes production that appears to be a beneficial adaptation to virus-induced lymphopenia. The loss of thymic reactivation might contribute to a worse prognosis.[97] Despite great importance of immunological dysregulation caused by T-cell deficiency, there were only a few studies with application of thymus derived medicines,[42,61,98] although the immune-modulating and protective effect of thymus extract has already been known for more than two hundred years.[99]

On June 16, 2020, Professor Peter Horby said, that dexamethasone "is the only drug so far that has been shown to reduce mortality – and it reduces it significantly".[100] It reduced deaths by one-third in patients receiving invasive mechanical ventilation, by one-fifth in patients receiving oxygen without invasive mechanical ventilation, but did not reduce mortality in patients not receiving respiratory support at randomization.[101] The later conclusion on the efficacy of corticosteroids was pessimistic: "There is no evidence that corticosteroids are safe and effective on the treatment of severe acute respiratory infection when COVID-19 disease is suspected".[102] The key point of these controversial claims was a wrong approach to use corticosteroids on patients with COVID-19. The corticosteroids should be recommended as a replacement therapy to the patients with bacterial or viral infectious disease being in the phase of exhaustion according to the general adaptation syndrome described by Hans Selye.[31-32,45] (Fig. 5.c) Thus, blood tests on cortisol and aldosterone must be obligatory routine analyses before prescription of corticosteroids therapy, especially in the case of COVID-19.

1.8. Case fatality ratio and infection fatality ratio

There are two most important characteristics of infectious diseases: the first is a case fatality ratio (CFR) and the second, an infection fatality ratio (IFR). Case fatality ratio is the proportion between the number of patients who died from COVID-19 and the number of confirmed cases of COVID-19, while infection fatality ratio is the proportion between the number of patients who died from COVID-19 and the number of estimated cases infected with SARS-CoV-19.[103]

To identify the total number of infection prevalence, tests were carried out for the presence of the viral genome – Polymerase chain reaction (PCR), or for specific antibodies against SARS-CoV-2 virus (IgM and IgG). Due to the fact that PCR provided positive results for a limited time after infection, and specific antibodies were produced and circulated in the blood of an infected person from several months up to a year,[104-105] the percentage of seroprevalence would always be lower than the real one, and, therefore, IFR from COVID-19 would be always overestimated.

In a study published by J. Ioannidis (2020), at the end of October 2020, the number of infected people worldwide reached 10%.[106] Similar proportion of infected people in October 2020 was calculated for Belgium, Brazil, and the United States.[107] In December 2020, the number of infected people in the United States was estimated at 50 million, or around 15%.[108]

On January 29, 2021, the Mayor of Moscow, Sergei Sobyanin announced that "half of Moscow's 12 million residents have had Covid-19" and recovered.[109] That estimation was based on a trial where antibodies to the SARS-CoV-2 virus were found in more than half of the blood samples taken randomly from a thousand *healthy* residents of Moscow.[110]

Thus, one may conclude that since the beginning of the pandemic, major populations of large cities have already been infected with SARS-CoV-2 and have some amount of circulated antibodies or have memory about this virus stored in the T-cells.[111-113]

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1.9. Databases were collected from Worldometer website

Information on cumulative numbers of the total cases and deaths due to COVID-19 is available at the Worldometer website from January 21, 2020.[18] (Fig. 6) On January 23, 2020, a controversial article on RT-PCR tests was published,[114] and a historical session of the World Economic Forum devoted to Wuhan Coronavirus took place in Davos.[115] Despite the fact that there was no cause for alarm yet,[116] January 23, 2020 was chosen as the first day of the current study.*

To provide an overall and detailed analysis of the COVID-19 pandemic, one year and a half was divided into three phases: (23.01.20-22.07.20), (23.07.20-22.01.21) and (23.01.21-22.07.21). Twenty three sets of databases, dated the 22nd of each month from January 2020 to November 2021, were collected. Raw data included more than 20,000 figures in total. Only simple calculations using MS Excel easily understandable by any doctor have been used.

The databases related to each month for every country were calculated by subtracting the previous month's data from the analyzed month's data. For example, in China on 22.02.20 there were 76,923 cases, and 2,441 deaths, and on 22.01.20 there were 571 cases and 17 deaths. Subtracting the second from the first, one gets that from 23.01.20 to 22.02.20 there were 76,352 cases and 2,424 deaths, and so on. The same method was used to count the database related to each phase for every country. Since only 213 countries† were affected by COVID-19 during the first phase, these 213 countries were analyzed during the current study.

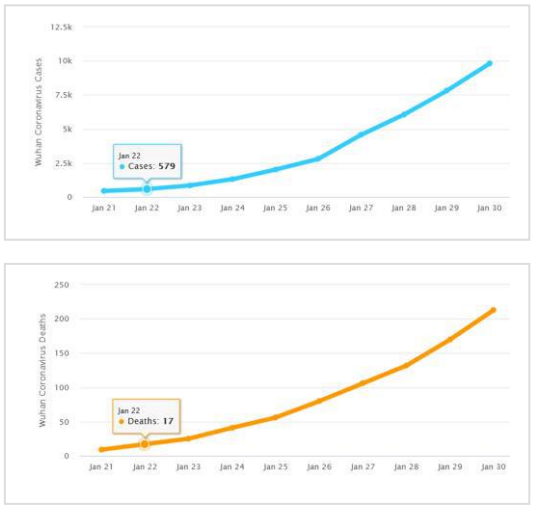

Figure 6. Cumulative numbers of the total cases of COVID-19, and the total deaths due to COVID-19 started on January 21, 2020; daily counts of both parameters have been available since January 22, 2020. [A part of the screenshot of the Worldometer website dated January 31, 2020, 21:35 GM].

* On January 23, 2020, Dr. Peter Salama, an expert in epidemiology, the former director of WHO's Health Emergencies Program, who organized a successful battle against the Ebola virus in the D.R.C., died suddenly.[117]

† Here and below 'Countries' means 'Countries and Territories'.

2. One and a half years of the pandemic: Case fatality ratio and infection fatality ratio

Objective

To evaluate CFR and IFR in 213 countries during one and a half years of COVID-19 pandemic.

2.1. Calculation of CFR among COVID-19 patients in 213 countries

Material and Methods

To calculate the CFR and IFR worldwide, the databases of 220 countries dated as July 22, 2021, 23:49 GMT, were collected at the Worldometer website. In these countries there were 193,349,043 confirmed cases of COVID-19; 4,150,541 deaths due to COVID-19; and a total population of 7,838,783,871 people.

Since in the first phase of COVID-19 pandemic (23.01.20-22.07.20) only 213 countries were affected, so databases of only these 213 countries were used for this study. Seven countries, including Marshall Islands, Micronesia, Saint Helena, Samoa, Solomon Islands, Vanuatu, and Wallis and Futuna, with 479 confirmed cases, 8 deaths, and population of 1,412,031 people were excluded from the study. In 213 countries there were 193,348,564 cases and 4,150,526 deaths.

A case fatality ratio was calculated by dividing the number of deaths by the number of confirmed cases.

Results

The overall case fatality ratio for 213 countries, counted by dividing the number of deaths (n=4,150,526) by the number of confirmed cases (n=193,348,564), was 2.147 %. The overall case fatality ratio for 220 countries was 2.147 % too.

2.2. Calculation of CFR among COVID-19 patients in 175 countries

Material and Methods

To increase the homogeneity of the main group of study, 38 countries with death numbers of fewer than 50 were excluded from further analysis. Thus, the main group of study decreased to 175 countries, with a total population of 7,734,426,580 people. These countries had 193,207,132 confirmed cases and 4,149,944 fatal cases. For each country, the CFR was calculated by dividing the number of deaths by the number of confirmed cases.

Results

The overall case fatality ratio for 175 countries was 2.148 %. In this group the CFR ranged from 0.267 % in Qatar to 19.597 % in Yemen, and the average value of CFR was 2.146±1.965%. Based on the calculated CFR values, all countries were divided into 16 groups as shown in Fig. 7.

The first group (n=7) where CFR was less than 0.500 %, included Qatar (0.267%), Maldives (0.285%), UAE (0.286%), Cyprus (0.418%), Seychelles (0.490%), Mongolia (0.495%), and Vietnam (0.498%).

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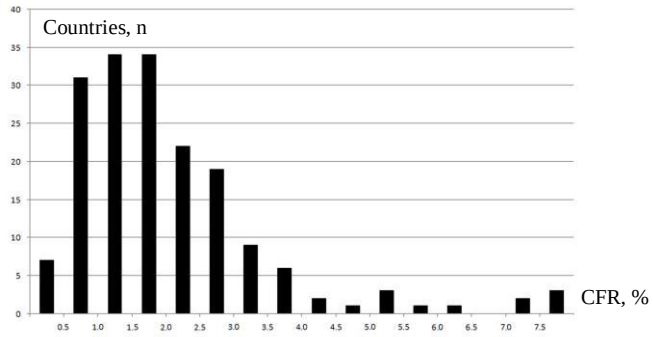

Figure 7. Distribution of 175 countries into 16 groups according to a CFR value
16 groups are: 1) CFR < 0.5%, n=7; 2) 0.5-1.0%, n=31; 3) 1.0-1.5%, n=34; 4) 1.5-2.0%, n=34; 5) 2.0-2.5%, n=22; 6) 2.5-3.0%, n=19; 7) 3.0-3.5%, n=9; 8) 3.5-4.0%, n=6; 9) 4.0-4.5%, n=2; 10) 4.5-5.0%, n=1; 11) 5.0-5.5%, n=3; 12) 5.5-6.0%, n=1; 13) 6.0-6.5%, n=1; 14) 6.5-7.0%, n=0; 15) 7.0-7.5%, n=2; 16) CFR>7.5%, n=3.

The groups # 9-16, where CFR exceeded 4.00 %, included 13 countries: Bulgaria (4.296%), Afghanistan (4.432%), Bosnia and Herzegovina (4.710%), China (5.017%), Taiwan (5.042%), Somalia (5.151%), Egypt (5.801%), Ecuador (6.415%), Syria (7.370%), Sudan (7.475%), Mexico (8.807%), Peru (9.316%), and Yemen (19.597%)

Conclusion

The calculations done in this section showed that in 38 out of 175 countries, CFR was less than 1.00%, in 68 countries CFR varied between 1.00% and 2.00%, and in 69 countries CFR was more than 2.00%. In 7 out of 175 countries, CFR was less than 0.50%.

2.3. Calculation of CFR among patients in 38 countries excluded from the main study

Background

As mentioned above, 38 countries were excluded from the main group of study.

Material and Methods

The group of countries excluded from the main study consisted of 8 countries without fatal cases related to COVID-19, and 30 countries where the number of fatal cases was from 1 to 49. In 30 countries with a total population of 102,945,260, there were 140,853 cases of COVID-19 and 582 deaths caused by COVID-19. For each country, a CFR was calculated.

Results

In 18 out of 30 countries CFR was less than 1.00% (including 10 with CFR < 0.50%), in 8 countries CFR was between 1.00% and 2.00%, and in the remaining 4 countries, CFR was more than 2.00%. Since there were no fatal cases due to COVID-19 in 8 countries, the CFR was less than 1.00% and less than 0.50%.

Conclusion

If the previous calculations done in section 2.2. were to be taken into account, then in 64 out of 213 countries, CFR was less than 1.00%; in 76 countries CFR varied between 1.00 and 2.00%; and in 73 countries, CFR was more than 2.00%. In 25 out of 213 countries, CFR was less than 0.50%.

2.4. Calculation of IFR among COVID-19 patients of 136 countries

Background

Before estimation of an infection fatality ratio, it was assumed that each person was tested only once, and the distribution of infected people among the entire population was equal. Therefore, the number of infected people was expected to increase in direct proportion to the increase in the number of new tests performed. The total number of infected people (IP) was derived from the number of total confirmed cases (C) divided by the total number of tests performed (T) and multiplied by the total population (P). Then, IFR was calculated by dividing the number of deaths due to COVID-19 (D) by the estimated number of people infected with the SARS-CoV-2 virus.

In the previous study[1] to estimate the number of infected people, a formula {IP=C•P/T} was used, but it was assumed that results of IFR {IFR=D/IP} would be overestimated. Further comparison of the results calculated using this formula, with the results estimated in other studies[106-108] revealed the consistency of the results with a difference of around 1.8 fold; so, a corrected formula was {IP = (C•P/T)•1.8}. The final adjusted formula used in the current study was IFR = [(D•T)/(C•P)]/1.8.

Material and Methods

After collecting the databases, countries with fewer than 50 reported cases of deaths, countries without information on the number of tests on SARS-CoV-2, and countries where the number of tests performed exceeded the total population, were excluded from the IFR study group.

The main group consisted of 136 countries with a total population of 6,864,034,602 people, 121,373,035 confirmed COVID-19 cases, 2,768,774 fatal cases related to COVID-19 and 1,370,764,127 COVID-19 tests. To calculate the number of infected people, a formula {IP=(C•P/T) •1.8} was used. To calculate infectious fatality ratio for each country a formula {IFR = [(D•T)/(C•P)]/1.8} was used.

Results

Since 121,373,035 COVID-19 cases were detected after 1,370,764,127 tests, it can be expected that if the number of tests would reach the total population (6,864,034,602), the number of infected people would increase up to 1,093,985,210. Thus, the overall IFR for 136 countries would be [(2,768,774• 1,370,764,127)/(121,373,035•6,864,034,602)]/1.8 = 0.253%.

Among 136 countries analyzed, the IFR ranged from 0.003% in the Democratic Republic of Congo (the minimal value) to 2.340% in Peru (the maximal value).

Based on the estimated IFR values, all the countries analyzed were divided into 16 groups, as illustrated in Fig. 8.

The first and largest group with the lowest value of IFR (< 0.10%) included 52 countries. Some of the countries had quite large populations, for example, Pakistan (225,392,516; 0.088%), Nigeria (211,492,907; 0.008%), Bangladesh (166,414,749; 0.040%), Ethiopia (117,947,327; 0.022%),

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Egypt (104,359,775; 0.095%); Vietnam (98,259,748; 0.033%), etc. But other countries in this group had small populations, for example, Seychelles (98,988; 0.059%), French Polynesia (282,617; 0.039%), Réunion (902,035; 0.049%), Equatorial Guinea (1,451,181; 0.090%), etc.

The groups # 11-16 with high values of IFR (>1.00%) included 8 countries: Slovakia (1.001%), Canada (1.030%), Germany (1.065%), Chile (1.134%), Bulgaria (1.207%), Hungary (1.343%), Australia (1.425%), and Peru (2.340%).

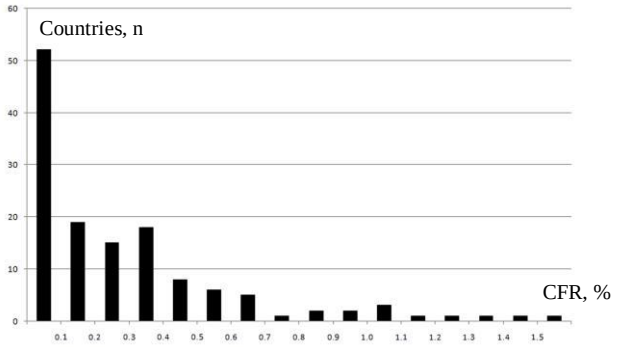

Figure 8. Distribution of 136 countries into 16 groups according to a IFR value 16 groups are: 1) IFR < 0.10%, n=52; 2) 0.10-0.20%, n=19; 3) 0.20-0.30%, n=15; 4) 0.30-0.40%, n=18; 5) 0.40-0.50%, n=8; 6) 0.50-0.60%, n=6; 7) 0.60-0.70%, n=5; 8) 0.70-0.80%, n=1; 9) 0.80-0.90%, n=2; 10) 0.90-1.00%, n=2; 11) 1.00-1.10%, n=3; 12) 1.10-1.20%, n=1; 13) 1.20-1.30%, n=1; 14) 1.30-1.40%, n=1; 15) 1.40-1.50%, n=1; 16) IFR > 1.50%, n=1.

Conclusion

The calculations done in this section showed that in 128 out of 136 countries, the IFR was below 1.00 %, in 7 countries IFR was between 1.00 and 2.00 %, and only in 1 country IFR were above 2.00 %. In 112 out of 136 countries IFR was less than 0.50 %.

2.5. Estimation of IFR in the 77 countries excluded from the main study

Background

As mentioned above, some countries were excluded from the main group of study.

Material and Methods

To estimate IFR for 52 countries, including 5 countries without information on the number of tests, and 47 countries where the number of tests performed exceeded the total population, a ratio between average CFR and average IFR in the main group of countries was calculated.

The main group (n=136) was divided into 4 subgroups: (1st) CFR was less than 1.00%, N=24; (2nd) CFR was between 1.00 and 2.00%, N=50; (3rd) CFR was between 2.00 and 3.00%, N=35; and (4th) CFR was higher than 3.00%, N=27. For each of these subgroups a ratio or a coefficient between average CFR and average IFR was counted: (1st) CFR/IFR=4.369; (2nd) CFR/IFR=5.991; (3rd) CFR/IFR=7.565; (4th) CFR/IFR=11.586. These four coefficients were used to calculate IFR in the group of 52 countries mentioned above.

In the group of countries (n=17) where the number of tests performed was higher than "0" but less than the population, and the number of deaths was less than 50, IFR was counted using the formula IFR = [(D•T)/(C•P)]/1.8, which was used in section 2.4.

Results

In 47 countries without information on the number of tests performed and 5 countries where the number of tests performed exceeded the total population (52 countries in total), the estimated IFR was less than 1.00%, including 51 countries, where IFR was less than 0.50%.

In all countries where the number of death was less than 50 (n=17), IFR was less than 1.00 %; and in 14 out of 17 countries, IFR was less than 0.50%.

In 8 countries without deaths, IFR was "0", so it was less than 1.00% and less than 0.50%.

Conclusion

The calculations done in the section 2.4 and 2.5 revealed that in 205 out of 213 countries, IFR was less than 1.00 %; in 7 countries IFR was between 1.00% and 2.00 %; and only in 1 country IFR was more than 2.00 %. In 185 out of 213 countries IFR was less than 0.50 %.

Taking into account the results of a study conducted in January, 2021, when 50 % of Moscow's city population had already antibodies against SARS-CoV-2,[109-110] one may assume that in July, 2021, the percentage of seroprevalence could be even higher and IFR could be lower than estimated in the current study.

2.6. Dynamics of the main cumulative data during 22 months of the COVID-19 pandemic

Background

The current pandemic curve has a wave-like form with a gradual increase and decrease of daily, weekly, and monthly numbers related to cases and deaths.

Material and Methods

Twenty three sets of databases, which were dated the 22nd of each month from January 2020 to November 2021, were collected. The number of total COVID-19 cases, deaths due to COVID-19, tests performed, and population were presented in Table 1. CFR, IFR as well as number of cases per 1 million (C/M) and death per 1 million (D/M) were counted for each date (Table 1). Dynamics of CFR and IFR were illustrated in Fig. 9.

Results

During 22 months of the pandemic there was an increase in the total number of cases, deaths, and tests on COVID-19 as well as population worldwide. Comparisons between numbers related to the pandemic collected on January 22, 2021 (12 months, or 1 year) and July 22, 2021 (18 months, or 1.5 years), revealed that during the six months, parameters of the pandemic were almost doubled compared to the

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similar cumulative parameters during the previous one year. The number of COVID-19 cases and deaths increased by 1.96 fold, and the number of tests increased by 2.13 fold.

The cumulative CFR was highest in April and May, 2020, followed by a decreasing trend, but the estimated cumulative IFR increased gradually (Fig. 9).

Table 1. Dynamics of the main cumulative data during 22 months of the COVID-19 pandemic

#	Date	Cases	Deaths	Tests	Population	CFR	IFR	C/M	D/M
0	22.01.20	579	17	-	-	2.936	-	-	-
1	22.02.20	78,001	2,457	-	-	3.150	-	-	-
2	22.03.20	334,886	14,603	-	-	4.361	-	-	-
3	22.04.20	2,632,559	183,879	23,282,447	-	6.985	-	-	-
4	22.05.20	5,296,813	339,374	67,673,680	7,749,928,184	6.407	0.031	683	44
5	22.06.20	9,176,001	473,406	130,810,378	7,756,390,179	5.159	0.048	1,183	61
6	**22.07.20**	**15,362,745**	**625,395**	**302,374,544**	**7,762,530,924**	**4.071**	**0.088**	**1,979**	**81**
7	22.08.20	23,358,160	807,665	409,774,283	7,768,876,378	3.458	0.101	3,007	104
8	22.09.20	31,750,352	974,050	609,767,516	7,775,221,824	3.068	0.134	4,084	125
9	22.10.20	41,959,098	1,142,057	759,449,532	7,781,362,578	2.722	0.148	5,392	147
10	22.11.20	58,947,048	1,392,963	955,296,514	7,787,708,023	2.363	0.161	7,569	179
11	22.12.20	78,280,842	1,721,802	1,164,332,290	7,793,848,775	2.200	0.183	10,044	221
12	**22.01.21**	**98,669,593**	**2,113,750**	**1,375,887,509**	**7,800,194,225**	**2.142**	**0.210**	**12,650**	**271**
13	22.02.21	112,239,378	2,484,426	1,589,416,906	7,806,539,667	2.214	0.250	14,378	318
14	22.03.21	124,265,956	2,734,688	1,805,314,644	7,812,271,038	2.201	0.283	15,907	350
15	22.04.21	145,297,992	3,083,902	2,087,974,472	7,818,616,492	2.122	0.315	18,584	394
16	22.05.21	167,027,095	3,467,994	2,378,274,484	7,825,090,334	2.076	0.350	21,345	443
17	22.06.21	179,871,406	3,896,149	2,660,800,034	7,831,231,088	2.166	0.409	22,968	498
18	**22.07.21**	**193,348,564**	**4,150,533**	**2,926,443,254**	**7,837,371,840**	**2.147**	**0.445**	**24,670**	**530**
19	22.08.21	212,552,947	4,443,846	3,218,070,808	7,843,921,989	2.010	0.477	27,098	567
20	22.09.21	230,824,305	4,731,461	3,598,394,533	7,850,062,735	2.050	0.522	29,404	603
21	22.10.21	243,676,239	4,952,263	3,889,118,661	7,856,203,486	2.032	0.559	31,017	630
22	22.11.21	258,262,254	5,172,861	4,212,580,383	7,862,548,934	2.003	0.596	32,847	658

Conclusion

During the last 6 months of the analyzed 1.5 years of the pandemic, the number of COVID-19 cases, deaths and tests was dramatically increasing. To provide a more detailed analysis of this negative trend, 1.5 years was divided into 3 phases: the 1st phase (23.01.20-22.07.20), the 2nd phase (23.07.20-22.01.21), and the 3rd phase (23.01.21-22.07.21), which are analyzed in the next section.

3. Three phases of the COVID-19 pandemic in 213 countries

Background

During six months of the 3rd phase (23.01.21-22.07.21) the number of cases, deaths and tests was almost equal to the similar ones reported during the previous one year (23.01.20-22.01.21).

Objective

To analyze and compare the dynamics of cases, deaths and tests during three phases of the pandemic.

Material and Methods

Analysis of the three phases of the COVID-19 pandemic was divided into two parts. The overall analysis in 213 countries was carried out in the first part, and a separate analysis of each country, – in the second part.

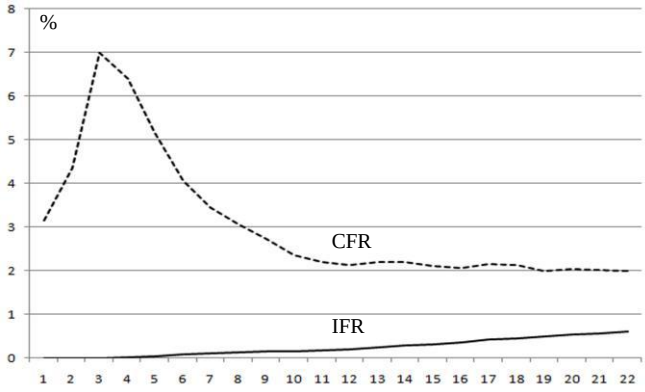

Figure 9. Dynamics of CFR and IFR during 22 months of the COVID-19 pandemic

3.1. Overall analysis of the three phases of the COVID-19 pandemic in 213 countries

Material and Methods

Four databases, dated 22.01.20, 22.07.20, 22.01.21 and 22.07.21 were collected from the Worldometer website. The number of cases, deaths, and tests related to each phase for each of the 213 countries was calculated by subtracting the previous phase's data from the analyzed phase's data. For example, on 22.01.21 there were 98,669,593 cases, 2,113,750 deaths, and 1,375,887,509 tests; and on 22.07.21 there were

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193,348,564 cases, 4,150,533 deaths, and 2,926,443,254 tests. Subtracting the first numbers (dated 22.01.21) from the second (dated 22.07.21), one concludes that during 6 months, from 23.01.21 to 22.07.21 there were 94,678,971 new cases, 2,036,783 new deaths, and 1,550,555,745 new tests, etc. CFR for each phase was calculated.

Ratios between cases, deaths and tests recorded during the 1st, 2nd and 3rd phases in relation to the similar parameters recorded during the whole 1.5 years were also counted. Additionally, a calculation of ratios between cases, deaths and tests recorded during 12 months of the first year of the pandemic in relation to the similar parameters recorded during the whole 1.5 years was also carried out. (Table 2).

Results

According to the calculations done, the 3rd phase was characterized by a dramatic increase for all parameters of the pandemic, including cases, deaths, and tests. The most intensive growing parameter was tests conducted to reveal new suspicious cases of COVID-19.

The case fatality ratio was the highest in the 1st phase, then decreased in the 2nd phase and again increased in the 3rd phase.

Table 2. Number of cases, deaths and tests related to 6 months of various phases, and also the same numbers recorded during the first 12 months (phases I+II, 1 year) and the whole period of 18 months (phases I+II+III, 1.5 years).

Phase, #	Date	Cases	%	Deaths	%	Tests	%	CFR,%
I	23.01.20-22.07.20	15,362,166	7.94	625,378	15.07	302,374,544	10.33	4.071
II	23.07.20-22.01.21	83,306,848	43.09	1,488,355	35.86	1,073,512,965	36.68	1.787
III	23.01.21-22.07.21	94,678,971	48.97	2,036,783	49.07	1,550,555,745	52.99	2.151
I+II+III	**23.01.20-22.07.21**	**193,348,564**	**100.0**	**4,150,533**	**100.0**	**2,926,443,254**	**100.0**	**2.147**
I+II	23.01.20-22.01.21	98,669,014	51.03	2,113,733	50.93	1,375,887,509	47.01	2.142
III	23.01.21-22.07.21	94,678,971	48.97	2,036,783	49.07	1,550,555,745	52.99	2.151
I+II+III	**23.01.20-22.07.21**	**193,348,564**	**100.0**	**4,150,533**	**100.0**	**2,926,443,254**	**100.0**	**2.147**

3.2. Analysis of the three phases of the COVID-19 pandemic for each of the 213 countries

Material and Methods

Four databases for each country, dated 22.01.20, 22.07.20, 22.01.21 and 22.07.21 were collected from the Worldometer website.

The number of cases, deaths, and tests related to each phase for every country was calculated by subtracting the previous phase's data from the analyzed phase's data. For example, in Malaysia, on 22.07.20 there were 123 deaths; on 22.01.21 there were 660 deaths, and on 22.07.21 there were 7,574 deaths in total. (Fig. 10). Subtracting 660 from 7,574, and 123 from 660, one concludes that during 6 months, from 23.01.21 to 22.07.21 there were 6,914 new deaths, and from 23.07.20 to 22.01.21, there were 537 deaths. A CFR was calculated for each country for every phase.

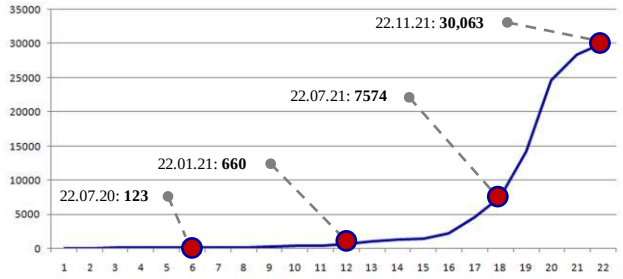

Figure 10. Dynamics of cumulative number of deaths in Malaysia.
The vertical axis shows number of deaths;
the horizontal axis shows number of a month.

Then a comparison between the number of cases, deaths, and tests recorded during the 3rd phase of the pandemic (23.01.21-22.07.21) and the number of similar parameters recorded during 1.5 years (23.01.20-22.07.21) was carried out for each country.

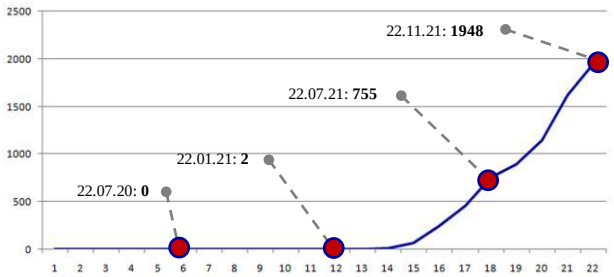

Figure 11. Dynamics of cumulative number of deaths in Mongolia.
The vertical axis shows number of deaths;
the horizontal axis shows number of a month.

For example, in Mongolia, at the end of the 2nd phase or one year of the pandemic (22.01.21), there were 2 deaths only; but at the end of the 3rd phase or 1.5 years of the pandemic (22.07.21), there were 755 deaths in total. (Fig. 11). After subtracting the first figure from the second, one can conclude that during 6 months of the 3rd phase of the pandemic there were 753 new deaths in Mongolia. If the a number of deaths for the 3rd phase (n=753) is divided by the number of deaths for 1.5 years of the pandemic (n=755), it can be concluded that during the 1.5 years of the pandemic, 99.74% of deaths due to COVID-19 in Mongolia took place during the 3rd phase of the COVID-19 pandemic.

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Table 3. (a) Distribution of countries according to CFR, and (b) average CFR during each phase of the COVID-19 pandemic

(a)							(b)	
		CFR, %					**Average CFR**, % in countries with fatal cases	
Phase	N	**> 2.0**	**1.0-2.0**	**< 1.0**	Including			
					< 0.50	0.00	Average CFR	Countries, N
I	213	110	39	64	41	28	3.597 ± 3.732	185
II	213	61	61	91	49	19	1.863 ± 2.616	194
III	213	68	72	73	37	16	2.025 ± 2.098	197

Results

Based on the CFR calculated for each phase, the 213 countries were divided into 3 groups (Table 3/a). A group of countries where CFR was less than 1.00% included countries with CFR less than 0.50% and with CFR=0.00%. An average CFR for each phase was calculated for countries (N) where fatal cases were recorded (Table 3/b).

Based on the comparison between numbers related to the 3rd phase and the whole period of 1.5 years, all the countries were divided into 6 groups (Table 4). If the ratio between numbers recorded during the 3rd phase and the numbers recorded during the whole 1.5 years of the pandemic is higher than 33.33 %, it means the number of cases, or deaths or tests recorded during the 3rd phase was higher than the average number for each of the three phases. If this ratio is higher than 50.00 %, it means that the vast majority of cases, or deaths or tests took place during the 3rd phase of the pandemic. The higher the percentage, the more cases, deaths or tests took place during the 3rd phase.

Table 4. Distribution of countries into six groups where more than one third of cases, deaths and tests took place during the 3rd phase of the COVID-19 pandemic

	Six groups of countries according to the ratio between the number of cases, deaths and tests recorded in the 3rd phase and the similar numbers recorded during 1.5 years.						Total number of countries (%) where ratio was more than 33.33%
	33.33-50 %	**50-60 %**	**60-70 %**	**70-80 %**	**80-90 %**	**90-100 %**	
Cases	71	43	29	15	8	14	**180** (84.51 %)
Deaths	50	43	19	14	14	17	**157** (73.71 %)
Tests	52	67	34	19	9	12	**193** (90.61 %)

A list of the countries where the vast majority (80-100%) of COVID-19 cases or deaths, or tests took place during the 3rd phase of the pandemic is presented in small font below.

Cases [80-90 %, n=8]: Anguilla, Antigua and Barbuda, Isle of Man, Malaysia, Maldives, Mauritius, Saint Lucia, and Sri Lanka; [90-100%, n=14]: British Virgin Islands, Cambodia, Cuba, Fiji, Laos, Mongolia, Papua New Guinea, Saint Kitts and Nevis, Seychelles, Taiwan, Thailand, Timor-Leste, Uruguay, and Vietnam.

Deaths [80-90 %, n=14]: Antigua and Barbuda, Barbados, Caribbean Netherlands, Curaçao, Eritrea, Namibia, Paraguay, Réunion, Saint Lucia, Somalia, St. Vincent Grenadines, Trinidad and Tobago, Uganda, Zambia; [90-100 %, n=17]: Botswana, British Virgin Islands, Cambodia, Cuba, Laos, Malaysia, Mongolia, Fiji, Papua New Guinea, Saint Kitts and Nevis; Seychelles, Sri Lanka, Taiwan, Thailand, Timor-Leste, Uruguay, and Vietnam.

Tests: [80-90 %, n=9]; Cyprus, Vietnam, Yemen, Turks and Caicos, Thailand, Denmark, Czechia, Timor-Leste, British Virgin Islands; [90-100 %, n=12]: Algeria, Austria, Burkina, Cameroon, Chad, DRC, Faso, Fiji, Sierra Leone, Somalia, Sudan, Syria; Taiwan.

Conclusion

Calculations done in this section have revealed that in most countries, the main number of cases, deaths and tests were recorded during the 3rd phase of the pandemic.

4. Twenty Two Months of the COVID-19 pandemic: Dynamics of cases, deaths, tests and CFR

Objective

To evaluate dynamics of monthly number of cases, deaths, and tests worldwide during 22 months of the COVID-19 pandemic, and to identify countries with the most dramatic tendency.

4.1. Twenty two months of the COVID-19 pandemic: Overall cases, deaths, tests and CFR worldwide

Objective

To evaluate dynamics of monthly numbers of cases, deaths, tests and CFR worldwide during 22 months of the COVID-19 pandemic

Material and Methods

Twenty three sets of databases, dated the 22nd of each month from January 2020 to November 2021, for 213 countries were collected. The databases related to each month for every country were calculated by subtracting the previous month's data from the analyzed month's data. The

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number of cases, deaths, tests as well as monthly ratios between cases and tests (C/T), deaths and tests (D/T), CFR, cases per 1 million (C/M) and deaths per 1 million (D/M) for all 213 countries together were counted and presented in Table 5. Monthly number of tests, cases, deaths illustrated in Figures 12-14.

Table 5. Monthly cases, deaths, and tests during 22 months of the COVID-19 pandemic worldwide. There are also ratios between number of cases and tests (C/T), number of deaths and tests (D/T), as well as CFR. The highest numbers in the column are highlighted in bold.

M,#	Date	Cases	Deaths	Tests	CFR	C/T	D/T	C/M	D/M
0	before 22.01.20	579	17	-	2.936	-	-	-	-
1	23.01.20 - 22.02.20	77,422	2,440	-	3.152	-	-	-	-
2	23.02.20 - 22.03.20	256,885	12,146	-	4.728	-	-	-	-
3	23.03.20 - 22.04.20	2,297,673	169,276	23,282,447	**7.367**	**9.869**	**0.727**	-	-
4	23.04.20 - 22.05.20	2,664,254	155,495	44,391,233	5.836	6.002	0.350	344	20
5	23.05.20 - 22.06.20	3,879,188	134,032	63,136,698	3.455	6.144	0.212	500	17
6	23.06.20 - 22.07.20	6,186,744	151,989	171,564,166	2.457	3.606	0.089	797	20
7	23.07.20 - 22.08.20	7,995,415	182,270	107,399,739	2.280	7.445	0.170	1,029	23
8	23.08.20 - 22.09.20	8,392,192	166,385	199,993,233	1.983	4.196	0.083	1,079	21
9	23.09.20 - 22.10.20	10,208,746	168,007	149,682,016	1.646	6.820	0.112	1,312	22
10	23.10.20 - 22.11.20	16,987,950	250,906	195,846,982	1.477	8.674	0.128	2,181	32
11	23.11.20 - 22.12.20	19,333,794	328,839	209,035,776	1.701	9.249	0.157	2,481	42
12	23.12.20 - 22.01.21	**20,388,751**	**391,948**	211,555,219	1.922	**9.638**	**0.185**	**2,614**	**50**
13	23.01.21 - 22.02.21	13,569,785	370,676	213,529,397	2.732	6.355	0.174	1,738	47
14	23.02.21 - 22.03.21	12,026,578	250,262	215,897,738	2.081	5.571	0.116	1,539	32
15	23.03.21 - 22.04.21	21,032,036	349,214	282,659,828	1.660	7.441	0.124	**2,690**	45
16	23.04.21 - 22.05.21	**21,729,103**	384,092	290,300,012	1.768	7.485	0.132	2,777	49
17	23.05.21 - 22.06.21	12,844,311	**428,155**	282,525,550	**3.333**	4.546	0.152	1,640	**55**
18	23.06.21 - 22.07.21	13,477,158	254,384	265,643,220	1.888	5.073	0.096	1,720	32
19	23.07.21 - 22.08.21	19,204,383	293,313	291,627,554	1.527	6.585	0.101	2,448	37
20	23.08.21 - 22.09.21	18,271,358	287,615	**380,323,725**	1.574	4.804	0.076	2,328	37
21	23.09.21 - 22.10.21	12,851,934	220,802	290,724,128	1.718	4.421	0.076	1,636	28
22	23.10.21 - 22.11.21	14,586,015	220,598	**323,461,722**	1.512	4.509	0.068	1,855	28

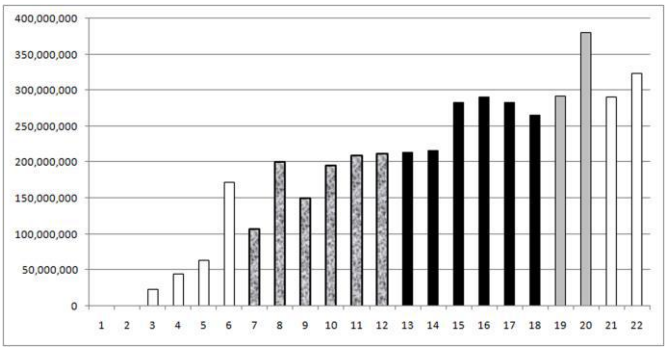

Figure 12. Monthly number of tests. The vertical axis shows number of tests; the horizontal axis shows number of a month. The 1st phase includes months # 1-6 (white columns); the 2nd phase includes months # 7-12 (grey-white columns); the 3rd phase includes months # 13-18 (black columns); months # 19-20th (grey columns); months # 21-22nd (white columns).

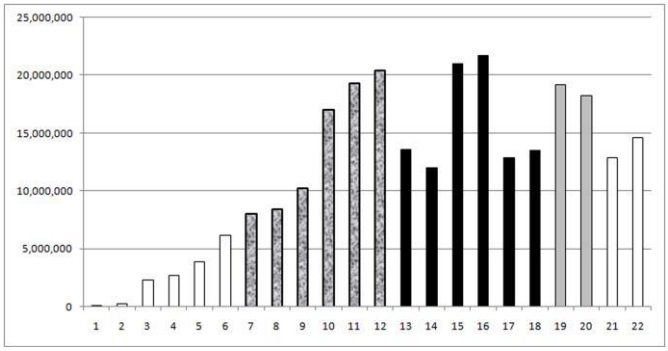

Figure 13. Monthly number of cases. The vertical axis shows number of cases; the horizontal axis shows number of a month. The 1st phase includes months # 1-6 (white columns); the 2nd phase includes months # 7-12 (grey-white columns); the 3rd phase includes months # 13-18 (black columns); months # 19-20th (grey columns); months # 21-22nd (white columns).

Results

During 22 months of the pandemic, the monthly number of tests increased almost gradually from 23,282,447 in the 3rd month, up to 380,323,725 in the 20th month (Fig. 12). The monthly number of cases varied from 77,422 in the first month up to 21,729,103 in the 16th month; there are three peaks, in the 11-12th, 15-16th and 19-20th months (Fig. 13). The monthly number of deaths varied from 2,440 in the first month up to 428,155 in the 17th month; there are two peaks, in the 12th month and in the 17th month (Fig. 14).

The highest monthly CFR (7.367) and the highest monthly ratio between cases and tests (9.869), as well as deaths and tests (0.727) were in the 3rd month (23.03.20-22.04.20) of the pandemic. Since March 11, 2020 the highest weekly CFR (8.507%) was estimated for the week April 12-18, 2020, and the highest daily CFR (9.514%) was estimated for April 17, 2020.[1]

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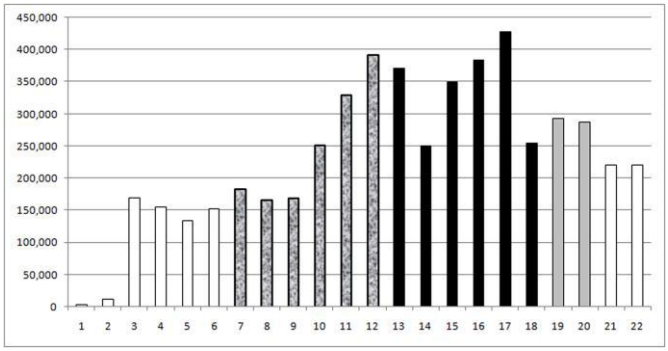

Figure 14. Monthly number of deaths. The vertical axis shows number of deaths; the horizontal axis shows number of a month. The 1st phase includes months # 1-6 (white columns); the 2nd phase includes months # 7-12 (grey-white columns); the 3rd phase includes months # 13-18 (black columns); months # 19-20th (grey columns); months # 21-22nd (white columns).

4.2. Evolution of the COVID-19 pandemic before and after the end of the 3rd Phase

Background

During 1.5 years of the pandemic, in the majority of the countries analyzed, number of COVID-19 cases, deaths and tests were highest during the 3rd phase.

Objective

To analyze the evolution of COVID-19 pandemic before and after the end of the 3rd phase

Material and Methods

Three databases for each country, dated 22.05.21, 22.07.21, and 22.09.21 were collected from the Worldometer website. Then, for each country, the cases, deaths and tests were calculated for 2 periods of time: (1st) 23.05.21-22.07.21 and (2nd) 23.07.21-22.09.21.

The trend of the pandemic was analyzed by dividing the numbers recorded during the 2nd period by the numbers recorded during the 1st period, accordingly. If the ratio is more than 1, i.e. more than 100 %, it means that after the end of the 3rd phase, there is still an upward trend in the number of COVID-19 cases, deaths, or tests in a certain country.

For example, in the United Kingdom, there were 127,716 total deaths on 22.05.21; 128,980 on 22.07.21, and 135,621 – on 22.09.21. (Fig. 15) Hence, there were 6,641 new deaths recorded during the 2nd period (23.07.21-22.09.21) and 1,264 new deaths recorded during the 1st period of time (23.05.21-22.07.21). Dividing 6,641 by 1,264 resulted in 5.225. That means, the number of deaths during the second period was more than five times higher than the number of deaths during the 1st period. Thus, in the United Kingdom there was a trend pointing to a dramatic increase in the number of deaths, etc.

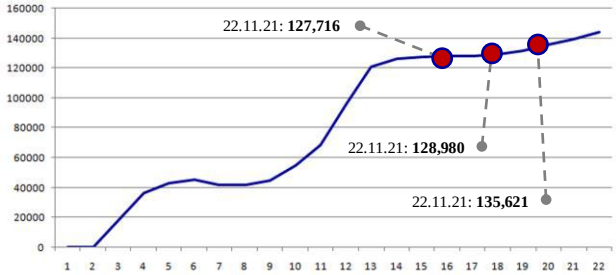

Figure 15. Dynamics of cumulative number of deaths in the United Kingdom. The vertical axis shows number of deaths; the horizontal axis shows number of a month.

Results

A comparison of the main parameters of the pandemic between the 2nd and 1st period of time for each country revealed that in the majority of them, there was an upward trend pointing to an increase in cases (n=158; 74.178%), deaths (n=133; 62.441%) and tests (n=125; 58.685%). Table 6.

Conclusion

A group of countries with a dramatic increase in COVID-19 cases, deaths, and tests during the 2nd period of time (23.07.21-22.09.21), in comparison with the 1st period 23.05.21-22.07.21), was revealed. In some of countries the difference between analyzed parameters exceeded 5-10 times, or even more. In three of them (Guadeloupe, Israel, Vietnam) there was a dramatic increase in all parameters including cases, deaths and tests.

Table 6. Results of a comparison between the number of cases, deaths and tests recorded in the databases of 213 countries during the 2nd (23.07.21-22.09.21) and the 1st (23.05.21-22.07.21) period of time.

#	Decrease / Increase	Cases		Deaths		Tests	
		N	%	N	%	N	%
1	Decrease (< 100%)	53	24.88	65	30.52	69	32.39
2	No change	2	0.94	15	7.04	19	8.92
3	Increase (> 100%)	158	74.18	133	62.44	125	58.69
	including:						
	from 0 to 1+n	4	01.88	16	07.51	3	01.41
	+ 100 – 200 %	46	21.60	38	17.84	91	42.72
	+ 200 - 500 %	54	25.35	46	21.60	24	11.27
	+ > 500 %	54	25.35	33	15.49	7	03.29
	Total	**213**	**100**	**213**	**100**	**213**	**100**

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A list of countries with a dramatic increase in COVID-19 cases, deaths, and tests between 23.07.21 and 22.09.21, is presented in small font below:

Increase in Cases [500-1000%; n=29]: Yemen, Austria, Estonia, Guinea-Bissau, Japan, USA, Ethiopia, Mauritius, Equatorial Guinea, Martinique, Laos, Burundi, Palestine, Morocco, Togo, Turks and Caicos, Moldova, Barbados, New Zealand, Eswatini, Somalia, Nigeria, Jamaica, Singapore, Greenland, Vietnam, Saint Lucia, Bulgaria, Sao Tome and Principe; [1000-2000%; n=8]: Bosnia and Herzegovina, Aruba, Montserrat, Romania, Iceland, Montenegro, Serbia, Azerbaijan; [>2000%; n=16]: Israel, Australia, San Marino, Guadeloupe, CAR, North Macedonia, Bermuda, Albania, Anguilla, French Polynesia, Antigua and Barbuda, Benin, Brunei, Dominica, New Caledonia, Grenada.

Increase in Deaths [by 500-1000%; n=17] Togo, the United Kingdom, North Macedonia, Kazakhstan, Timor-Leste, Libya, Benin, Belize, Curaçao, Singapore, Saint Lucia, Eswatini, Nigeria, Azerbaijan, Gambia, Guinea-Bissau, Ghana; [1000-2000%; n=8] Bermuda, Albania, Ivory Coast, Barbados, Morocco, Malta, Burundi, Israel; [>2000%; n=8] Mauritius, Somalia, Aruba, Guadeloupe, Vietnam, Australia, Martinique, French Polynesia.

Increase in Tests [by 300-500%; n=5] Israel, Vietnam, South Sudan, Falkland Islands, Guadeloupe; [>500%; n=7] Saint Pierre Miquelon, Brunei, Bhutan, Dominica, Timor-Leste, Thailand, Réunion.

4.3. Comparison of the average monthly number of cases, deaths and tests in each of the 213 countries related to the months # 21-22 (23.09.21-22.11.21) and to the previous two months # 19-20 (23.07.21-22.09.21).

Objective

To evaluate the dynamics of the monthly number of cases, deaths and tests in each of the 213 countries during the months # 19-22 of the COVID-19 pandemic, and to identify countries with a negative trend.

Material and Methods

The average number of monthly cases, deaths and tests were counted for two months # 21-22 (23.09.21-22.11.21) and for the previous two months # 19-20 (23.07.21-22.09.21). Then a comparison of these parameters was done by dividing the numbers related to the months # 21-22 by the numbers related to the previous two months # 19-20. If the ratio was more than 1, i.e. more than 100 %, it means that in a certain country, there was a trend pointing to an increase in COVID-19 cases, deaths, or tests. If the ratio was less than one (<100%), it means that the parameters of the pandemic had a downward trend - to decrease. Results are presented in Table 7.

Results

Despite the majority of countries analyzed showing lower average monthly number of cases, deaths, and tests in the last two months (# 21-22), compared with the same parameters recorded during the previous two months (# 19-20), there was a group of countries where the average monthly cases and deaths during the latest months were at least 5 times higher than during the previous two months; and the monthly number of tests during the latest months was at least 2 times higher than during the previous two months. The following list in small font included only countries with a total population of more than 3,000,000 people.

Increase in Cases [>500%; n=11] Cameroon (526%), Croatia (536%), Romania (713%), Ukraine (844%), Singapore (973%), Papua New Guinea (1033%), Slovakia (1643%), Czechia (2037%), Hungary (2066%), Poland (2537%), Tanzania (2897%).

Increase in Deaths [>500%; n=19] Egypt (504%), Austria (546%), Moldova (565%), Croatia (625%), Niger (643%), Congo (987%), Cameroon (1058%), Laos (1064%), Ukraine (1115%), Romania (1214%), Burkina Faso (1271%), New Zealand (1300%), Papua New Guinea (1370%), Czechia (1744%), Poland (1817%), Singapore (1856%), Tanzania (2334%), Slovakia (2418%), Hungary (2463%).

Increase in Tests [>200%; n=8] Slovenia (213%), Israel (219%), Greece (219%), Ukraine (226%), Hungary (235%), Germany (256%), Brazil (260%), Thailand (533%).

Conclusion

A comparison of the data related to the months # 21-22 and to the previous two months # 19-20 revealed a trend showing a decrease in the number of cases, deaths and tests. Nevertheless, there emerged a group of countries where the main parameters of the pandemic still had a tendency to increase.

Table 7. Results of a comparison between the average monthly number of cases, deaths and tests recorded during two months # 21-22 (23.09.21-22.11.21) and during the previous two months # 19-20 (23.07.21-22.09.21).

#	Decrease / Increase	Cases		Deaths		Tests	
		N	%	N	%	N	%
1	Decrease (< 100%)	129	60.56	108	50.70	124	58.22
2	No change	2	0.94	10	4.70	25	11.74
3	Increase (> 100%)	82	38.50	95	44.60	64	30.04
	including:						
	from 0 to 1+n	0	00.00	5	02.35	3	01.41
	+ 100 – 200 %	32	15.03	29	13.62	51	23.94
	+ 200 - 500 %	35	16.43	33	15.49	8	03.75
	+ > 500 %	15	07.04	28	13.14	2	00.94
	Total	**213**	**100**	**213**	**100**	**213**	**100**

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4.4. Comparison of the average monthly number of cases, deaths and tests in each of the 213 countries related to the latest month analyzed # 22 (23.10.21-22.11.21) and the previous month # 21 (23.09.21-22.10.21)

Objective

To evaluate the dynamics of the monthly number of cases, deaths and tests in each of the 213 countries during the months # 21-22, and to identify countries with a negative tendency.

Material and Methods

The number of monthly cases, deaths and tests for the months # 22 (23.10.21- 22.11.21) and # 21 (23.09.21-22.10.21) was counted in the same manner as in the previous sections. A comparison between two months was done by dividing the numbers related to month # 22nd by the numbers related to the month # 21st. If the ratio is more than 1, i.e. more than 100 %, there is still an upward trend in the number of COVID-19 cases, deaths, or tests in a certain country. If the ratio is less than one (<100%), it means parameters of the pandemic had a tendency to decrease. Results are presented in Table 8.

Results

A comparison of the data related to the month # 22 with the data related to the previous month (# 21) revealed a trend showing a decrease in number of cases, deaths and tests. Nevertheless, there are groups of countries where the monthly numbers of cases and deaths during the month # 22 was at least 5 times higher than during the previous month # 21; and the monthly number of tests during the month # 22 was at least 2 times higher than during the previous month # 21. The following list in small font included only countries with a total population of more than 3,000,000 people.

Increase in Cases [>500%; n=3] Poland (638%), Czechia (803%), Hungary (733%).

Increase in Deaths [>500%; n=5 Poland (535%), Hungary (768%), Niger (800%), Czechia (1075), New Zealand (1200%).

Increase in Tests [>200%; n=7] Nigeria (204%), Iran (211%), Hungary (220%), Haiti (250%), Argentina (236%), Germany (290%), Denmark (308%).

Conclusion

The study done in this section has revealed that during the months # 21-22 in the majority of countries analyzed, the number of new COVID-19 cases, deaths and tests had shown a tendency to decrease. This is an objective basis for optimism and inspires hope for an end to the pandemic.

Table 8. Results of a comparison between the monthly number of cases, deaths and tests recorded during the month # 22 (23.10.21-22.11.21) and the previous month # 21 (23.09.21-22.10.21)

#	Decrease / Increase	Cases		Deaths		Tests	
		N	%	N	%	N	%
1	Decrease (< 100%)	118	55.40	117	54.93	96	45.07
2	No change	6	2.82	16	7.51	40	18.78
3	Increase (> 100%)	89	41.78	80	37.56	77	36.15
	including:						
	from 0 to 1+n	0	00	10	04.69	9	04.23
	+ 100 – 200 %	48	22.53	49	23.01	57	26.76
	+ 200 - 500 %	35	16.43	16	07.51	10	04.69
	+ > 500 %	6	02.82	5	02.35	1	00.47
	Total	**213**	**100**	**213**	**100**	**213**	**100**

5. Discussion

An analysis of the main epidemiological parameters worldwide has resulted in distinguishing three phases of the pandemic worldwide: these phases are different in terms of the number of new tests, cases and deaths, and they have their own features in each country.

The first phase (23.01.20-22.07.20) began with new cases and first victims of COVID-19 identified outside China. During the first phase, diagnostic tests to detect SARS-CoV-2 were used mainly on people with symptoms and their immediate contacts. Clinical trials of potentially effective drugs were in the initial phase, and invasive mechanical ventilation, which had no therapeutic effect on patients with COVID-19, was used very actively. Since protocols of treatment were not developed yet, and the number of confirmed cases was small, the CFR value was the highest in the history of the pandemic.

During the second phase (23.07.20-22.01.21) clinical trials were completed and doctors received effective protocols of treatment.[65,82,85] Despite the emergence of new variants of the virus, mechanisms of the disease development remained unchanged and were not associated with a more severe course of the disease.[118-119] In most countries the mortality rate was very low. By the end of the second phase, worldwide statistics indicated the imminent end of the pandemic.[1]

During the third phase (23.01.21-22.07.21) of the pandemic, in various countries, mass vaccination was introduced to protect people against SARS-CoV-2. Coincidentally, a sudden rise in the number of new cases and deaths happened, and it could not be explained rationally. The highest number of monthly deaths was recorded between May 23, and June 22, 2021. The most dramatic evolution of the epidemic curve occurred in the countries where doctors had successfully battled COVID-19 during the first year of the pandemic [see

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appendix: Cambodia, Cuba, Laos, Malaysia, Mongolia, the Seychelles, Singapore, Shi Lanka, Taiwan, Tanzania, Thailand, Uruguay, Vietnam, etc.]. The further evolution of the pandemic was an undulating continuation of the third phase.

A group of countries where more than 90 % of deaths were recorded during the third phase included Botswana, British Virgin Islands, Cambodia, Cuba, Laos, Malaysia, Mongolia, Fiji, Papua New Guinea, Saint Kitts and Nevis; Seychelles, Sri Lanka, Taiwan, Thailand, Timor-Leste, Uruguay, and Vietnam.

After the end of the 3rd phase, during the next two months (#19-20) in the majority of countries analyzed, the number of deaths continued to increase. Dramatic increases in deaths during these months took place in the following countries: Albania, Aruba, Australia, Azerbaijan, Barbados, Belize, Benin, Bermuda, Burundi, Curaçao, Eswatini, French Polynesia, Gambia, Ghana, Guadeloupe, Guinea-Bissau, Ivory Coast, Israel, Kazakhstan, Libya, Malta, Martinique, Mauritius, Morocco, Nigeria, North Macedonia, Singapore, Saint Lucia, Somalia, Timor-Leste, Togo, the United Kingdom, and Vietnam.

In the following countries the number of deaths continued to increase even during the latest month analyzed (# 22): Burkina Faso, Cameroon, Congo, Djibouti, Gabon, Hungary, Laos, Latvia, Lesotho, Papua New Guinea, Poland, Romania, Singapore, Slovakia, South Sudan, Tanzania, Ukraine, etc.

6. Conclusions

Two years have passed since the Wuhan Municipal Health Commission announced a pneumonia epidemic. Despite the positive dynamics during October-November 2021, the current pandemic is not over yet, and additional research is necessary to identify the cause of the increase in the number of new cases and deaths observed during the third phase of the pandemic.

6.1. After simulating a forecast done by Neil M. Ferguson and his team (*Imperial College London*) in March 2020,[120] many countries introduced social distancing, quarantines and lockdowns. Despite objections to Mr. Ferguson's calculations from his own colleagues,[121] and the United Kingdom's removal of COVID-19 from the category of high consequence infectious disease,[122] quarantine measures were continued. As far as medical prophylactic measure in the form of global vaccination program is concerned, it had already been proposed before the new disease got its name.[115,123]

There are plenty of studies which revealed that in certain cases, various prophylactic measures used to prevent the spread of SARS-CoV-2 and other viruses and bacteria, could have negative effects on the human body,[124-225] have low efficacy or may even be useless in terms of prevention of diseases.[226-253]

Since the main target for SARS-CoV-2 are people with weak immunity,[13,40-42] and prolonged mental stress affects both the entire body,[124-126,254] and the immune system in particular,[255-259] a new study is needed to answer the question, if medical and non-medical measures used to prevent the spread of SARS-CoV-2 could affect natural immunity. This question is especially relevant for countries which had a dramatic increase in cases and deaths during the third phase of the pandemic. An affirmative answer to this question is highly probable since certain types of medical prophylactic products can reprogram immune system response,[163] and without a new dose of a booster immunity of the body declines after 3-6 months.[252] Moreover, there has been a tendency towards an increase in herpes zoster cases,[260-270] and "*the link between compromised immunity and herpes zoster has been recognized for more than half a century*".[271-272]

Since the list of criteria for exclusion from clinical trials with anti-SARS-CoV-2 vaccines included people who had received immune-modifying drugs,[273] due to early immunologic response to vaccination,[274] and people who have natural durable specific immunity after recovery from COVID-19,[275-284] these two groups of people should be analyzed separately, and at least four groups of studies are necessary, including:

1) unvaccinated people who have not received immuno-modulatory drugs;

2) unvaccinated people who have received immuno-modulatory drugs;

3) unvaccinated people who recovered from COVID-19 spontaneously or after treatment;

4) vaccinated people who received one, two or more doses of vaccine and boosters.

6.2. In July 2021 it was announced that after December 31, 2021, CDC would withdraw the request to the U.S. Food and Drug Administration for Emergency Use Authorization of the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel.[285]

Previously, some experts had already rejected the reliability and validity of the RT-PCR test to be used for screening.[286-289] That decision has been done to avoid negative epidemic consequences of the false positive results which could be caused by contamination of the environment[290-294] or test kits,[288,295-301] by the limitations of the diagnostic method itself,[302] and errors of the software used,[303] as well as by application of a cycle threshold of 25-30 or higher.[304-306]

A number of false positive results could be dramatically increased if the RT-PCR test is used to conduct large-volume screening at the area of low prevalence of SARS-CoV-2.[307-309] Thus, mass-screening with RT-PCR test could create a false epidemic without a real basis.[310]

At the time when Dr. Tedros A. Ghebreyesus assumed the outbreak of the pandemic,[48] objective data for such a decision was not available yet. Therefore, no official documents were issued and published. Five days later, Dr. Ghebreyesus explained that WHO did not know how many people were infected, and invited all countries to fill up this informative gap, by suggesting: "We have a simple message for all countries: test, test, test".[311] Mass testing resulted in sudden outbreaks of COVID-19 in many countries and this fact could not be explained rationally based on the natural evolution of infectious diseases.[312]

Since the recent study by S. Shah, A. Stang, et al (2021) revealed that application of mass screening with RT-PCR test had no value to predict severe cases or deaths,[289,313] an additional study is required to answer the question – if screening with RT-PCR test can increase the number of deaths, especially in countries where quarantine facilities do not provide isolated rooms for each person suspected to be infected.[314-316]

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6.3. One can assume that the application of non-specialized premises for quarantine and treatment of people suffering from infectious diseases can lead to unpredictable consequences. For example, the conversion of a new general municipal hospital (#40) in Moscow City into a specialized hospital for COVID-19 patients without reconstructions according to the hygienic requirements for infectious hospitals resulted in the steady increase in hospital mortality. (Fig. 16) Three fourths of the patients died due to sepsis caused by *K. Pneumoniae*, *A. Baumannii*, *P. Aeruginosa*, *E. Coli*, *S. Aureus*, fungus, etc.[317]

Since these data were presented by the head physician of the modern and well equipped hospital, one can assume that mass mortality from nosocomial infection was a common occurrence in COVID-19 hospitals worldwide.[318-322]

Therefore, a thorough investigation of the causes of death is necessary to distinguish between deaths from COVID-19 and deaths from other causes. Many statistical errors caused by imperfect diagnostics and registration are likely would be found.[250,323-325]

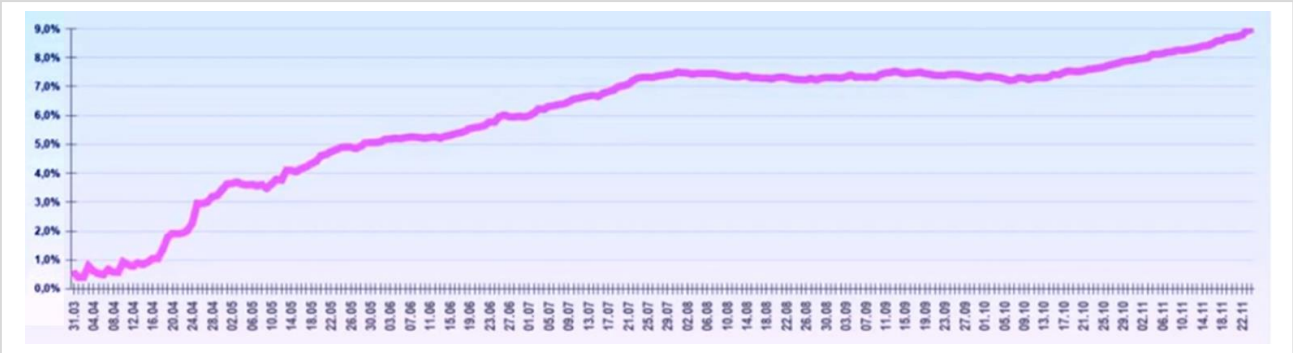

Figure 16. A steady increase in mortality in the leading anti-COVID-19 hospital in Moscow City.[317]

6.4. A comparison of different therapeutic methods and protocols used during the current pandemic should be done to identify the most effective ones.[65,82,85,86,326-329] An equally important task is to analyze information on the preventive effects of certain drugs, food supplements, vitamins and microelements.[330-347] This analysis should be carried out by experts in the appropriate field who have already demonstrated low mortality using their therapeutic protocols, but not by an outside reviewer who has no practical experience with analyzed remedies and who selects and rejects publications using an unprofessional view of the reviewed remedy or method. Otherwise, we can get negative results which we have already been warned by I. Prigogine et al., (1984): "what for generations had been a source of joy and amazement withers at its touch" (in this quote 'it' – means *the spirit of science*).[348] Global negative consequences of unprofessional review of the topic can be demonstrated by the example of the use of hydroxychloroquine and chloroquine, where reviewers "*were unable to confirm a benefit*" of these effective drugs.[84]

Thus, only complete information regarding the positive and negative impact[349] of medical and non-medical methods of diagnostics and prophylaxis of COVID-19 can help to organize effective measures to end the current pandemic and prevent a similar one from occurring in the future.

Presumably, there are several causes of the negative evolution of the current pandemic including (1) overreliance on PCR tests, (2) application of non-specialized premises for quarantine and treatment, (3) following therapeutic protocols used in countries with high number of deaths, (4) decrease in individual and herd immunity and (5) ignoring prophylactic treatment.

It can be suggested that the use of immunomodulatory drugs (for example, thymus extract or thymic peptides) should be included in the treatment of people with compromised T-cell immunity. Prophylactic as well as therapeutic protocols should also be changed from the 'standard' to 'personalized' ones.

Appendix includes illustrations for the following countries: Australia, Azerbaijan, Belarus, Cambodia, Cuba, Czechia, Denmark, Finland, Germany, Hungary, India, Indonesia, Israel, Italy, Japan, Kazakhstan, Laos, Malaysia, Mongolia, Morocco, Namibia, Norway, Paraguay, Russia, Poland, the Seychelles, Singapore, South Korea, Spain, Sri Lanka, Sweden, Taiwan, Tanzania, Thailand, Ukraine, the United Kingdom, the United States, Uruguay, Vietnam, Zimbabwe.

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Remark: A list of the references includes some articles or manuscripts, which have not been peer reviewed yet, or were published and then retracted. They are not recommended to doctors who have not enough knowledge and experience to evaluate the quality of a study.

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Appendix - Illustrations

Dynamics of the number of deaths during 22 months of the pandemic in various countries

Twenty three sets of databases, which dated the 22nd of each month from January 2020 to November 2021, were collected. The databases related to each month for every country were calculated by subtracting the previous month's data from the analyzed month's data. CFR, IFR, number of cases per 1 million (C/M) and death per 1 million (D/M) were counted.

Cumulative and Monthly number of cases, deaths, tests, CFR, C/M, D/M and population were presented in the form of a table (see an example for Australia). Graph illustrations for various countries included (a) Dynamics of cumulative number of deaths during 22 months of the COVID-19 pandemic; and (b) Monthly number of deaths due to COVID-19 during the pandemic.

These illustrations could help doctors of the respective countries to understand their errors that have led to an increase in the number of new cases and deaths, and to correct them.

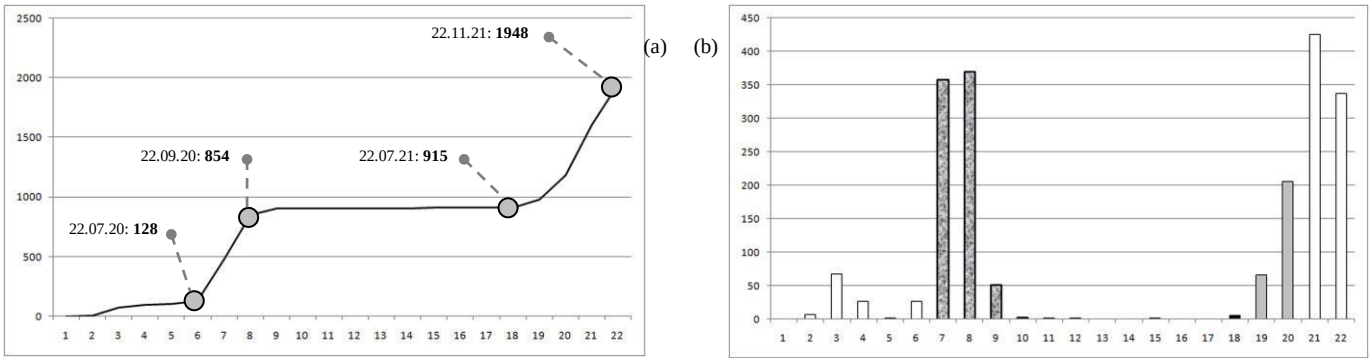
Australia

a) Cumulative number of cases, deaths, tests, population, CFR, IFR, C/M, D/M

#	Date	Cases	Deaths	Tests	Population	CFR	IFR	C/M	D/M
0	22.01.20	-	-	-	-	-	-	-	-
1	22.02.20	21	0	0	0	0	-	-	-
2	22.03.20	1353	7	0	0	0.517	-	-	-
3	22.04.20	6649	74	452441	0	1.113	-	-	-
4	22.05.20	7095	101	1170682	25466640	1.424	0.036	278.60	3.97
5	22.06.20	7474	102	2105974	25491691	1.365	0.063	293.19	4.00
6	22.07.20	12894	128	3641780	25515934	0.993	0.079	505.33	5.02
7	22.08.20	24602	485	5646546	25540986	1.971	0.242	963.24	18.99
8	22.09.20	26942	854	7351283	25566037	3.170	0.506	1053.82	33.40
9	22.10.20	27466	905	8420326	25590280	3.295	0.602	1073.30	35.37
10	22.11.20	27821	907	9713327	25615331	3.260	0.687	1086.11	35.41
11	22.12.20	28219	908	10720719	25639574	3.218	0.747	1100.60	35.41
12	22.01.21	28755	909	12642312	25664626	3.161	0.865	1120.41	35.42
13	22.02.21	28930	909	14089305	25689677	3.142	0.957	1126.13	35.38
14	22.03.21	29205	909	15209275	25712304	3.112	1.023	1135.84	35.35
15	22.04.21	29588	910	16481110	25737355	3.076	1.094	1149.61	35.36
16	22.05.21	30003	910	17797116	25762406	3.033	1.164	1164.60	35.32
17	22.06.21	30366	910	19821498	25786649	2.997	1.280	1177.59	35.29
18	22.07.21	32426	915	23457810	25810892	2.822	1.425	1256.29	35.45
19	22.08.21	44034	981	29437845	25836752	2.228	1.410	1704.32	37.97
20	22.09.21	90391	1186	36219104	25860995	1.312	1.021	3495.26	45.86
21	22.10.21	154489	1611	41907968	25885238	1.043	0.938	5968.23	62.24
22	22.11.21	199659	1948	46696043	25910289	0.976	0.977	7705.78	75.18

b) Monthly number of cases, deaths, tests, CFR, C/M, D/M

#	Date	Cases	Deaths	Tests	CFR	C/M	D/M
0	before 22.01.20	0	0	0	0	0	0
1	23.01.20 - 22.02.20	21	0	0	0	-	0
2	23.02.20 - 22.03.20	1332	7	0	0.526	-	-
3	23.03.20 - 22.04.20	5296	67	452441	1.265	-	-
4	23.04.20 - 22.05.20	446	27	718241	6.054	17.51	1.06
5	23.05.20 - 22.06.20	379	1	935292	0.264	14.87	0.04
6	23.06.20 - 22.07.20	5420	26	1535806	0.480	212.42	1.02
7	23.07.20 - 22.08.20	11708	357	2004766	3.049	458.40	14.00
8	23.08.20 - 22.09.20	2340	369	1704737	15.769	91.53	14.43
9	23.09.20 - 22.10.20	524	51	1069043	9.733	20.48	2.00
10	23.10.20 - 22.11.20	355	2	1293001	0.563	13.86	0.08
11	23.11.20 - 22.12.20	398	1	1007392	0.251	15.52	0.04
12	23.12.20 - 22.01.21	536	1	1921593	0.187	20.88	0.04
13	23.01.21 - 22.02.21	175	0	1446993	0	6.81	0.00
14	23.02.21 - 22.03.21	275	0	1119970	0	10.70	0.00
15	23.03.21 - 22.04.21	383	1	1271835	0.261	14.88	0.04
16	23.04.21 - 22.05.21	415	0	1316006	0	16.11	0.00
17	23.05.21 - 22.06.21	363	0	2024382	0	14.08	0.00
18	23.06.21 - 22.07.21	2060	5	3636312	0.243	79.81	0.19
19	23.07.21 - 22.08.21	11608	66	5980035	0.569	449.28	2.55
20	23.08.21 - 22.09.21	46357	205	6781259	0.442	1792.55	7.93
21	23.09.21 - 22.10.21	64098	425	5688864	0.663	2476.24	16.42
22	23.10.21 - 22.11.21	45170	337	4788075	0.746	1743.32	13.01



a) Dynamics of cumulative number of deaths in Australia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Australia.
The 1st phase includes months # 1-6 (white columns); the 2nd phase includes months # 7-12 (grey-white columns);
the 3rd phase includes months # 13-18 (black columns); months # 19-20th (grey columns); months # 21-22nd (white columns);
The vertical axis shows number of cases (a) or deaths (b); the horizontal axis shows number of a week.

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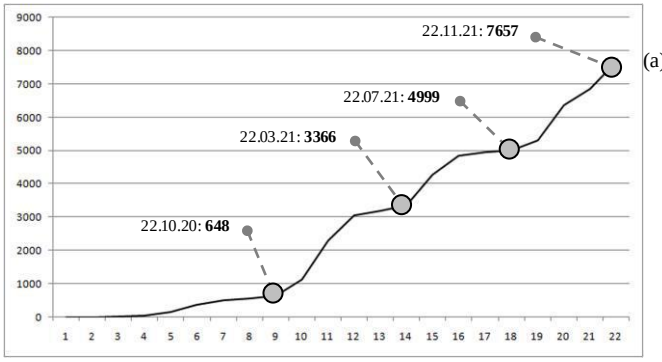
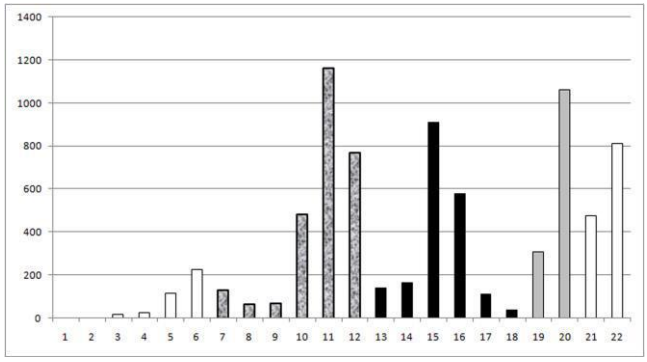
Azerbaijan

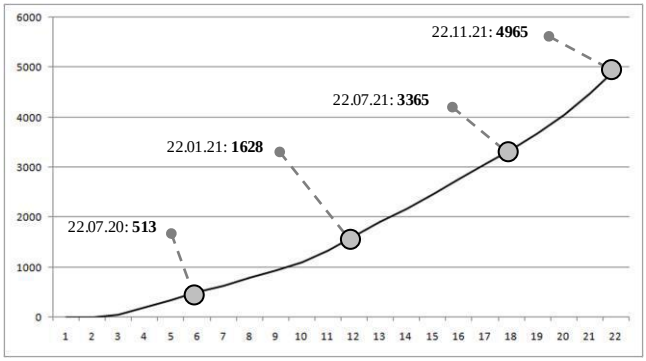


(a) (b)

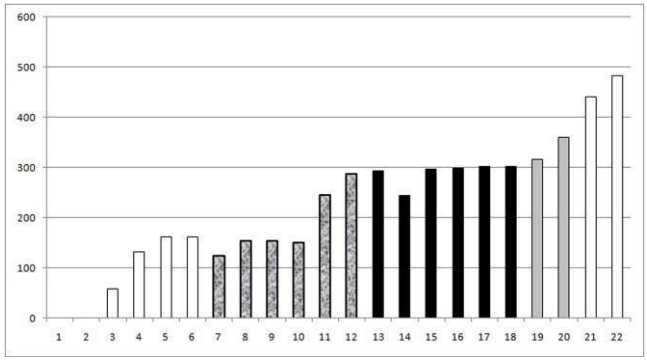


a) Dynamics of cumulative number of deaths in Azerbaijan during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Azerbaijan .

Belarus

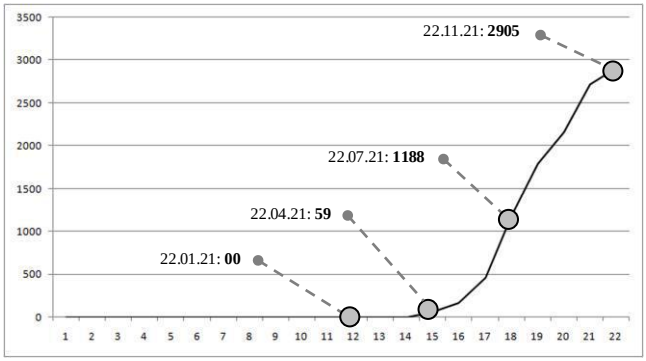


(a) (b)

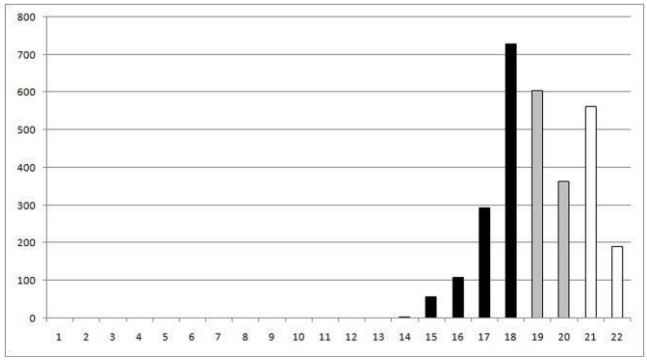


a) Dynamics of cumulative number of deaths in Belarus during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Belarus.

Cambodia



(a) (b)



a) Dynamics of cumulative number of deaths in Cambodia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Cambodia.

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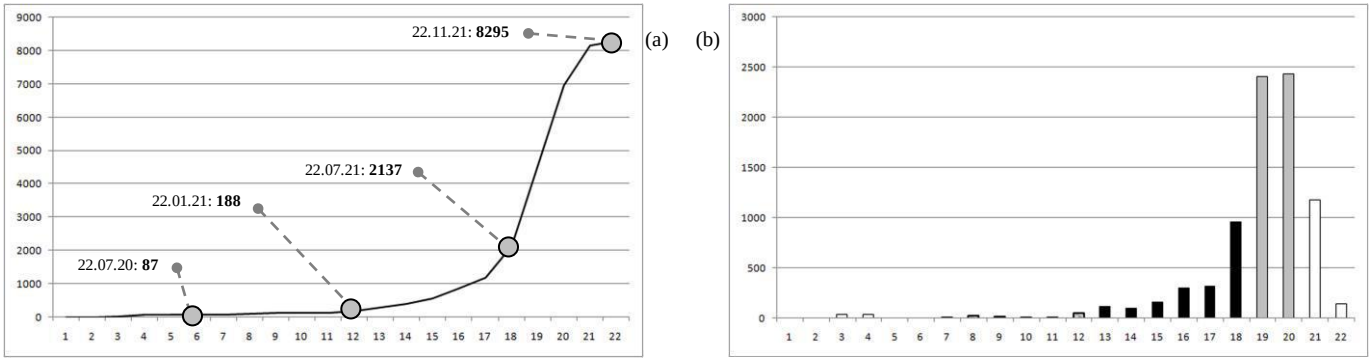
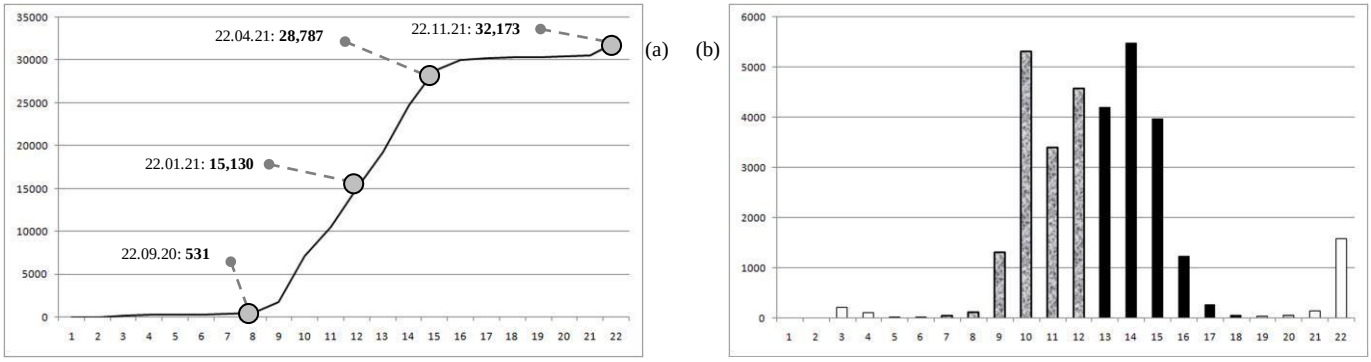
Cuba



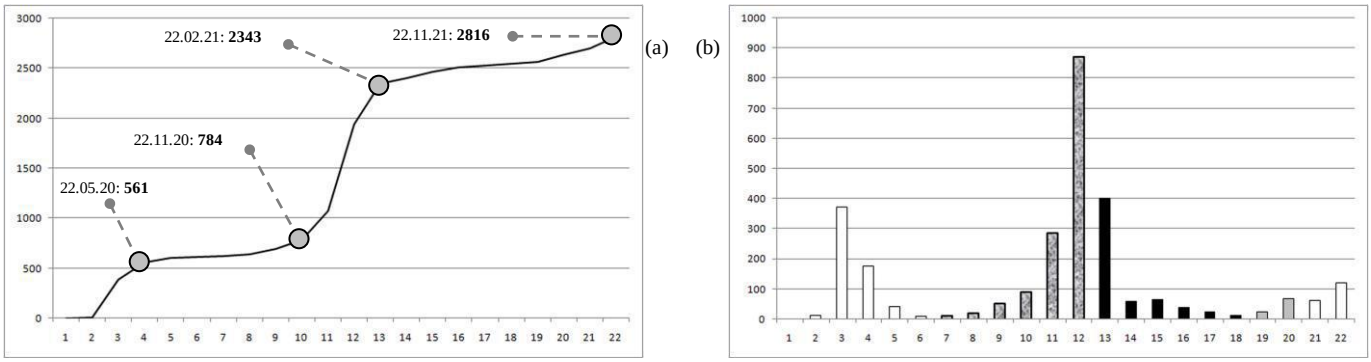
a) Dynamics of cumulative number of deaths in Cuba a during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Cuba.

Czechia



a) Dynamics of cumulative number of deaths in Czechia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Czechia.

Denmark



a) Dynamics of cumulative number of deaths in Denmark during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Denmark.

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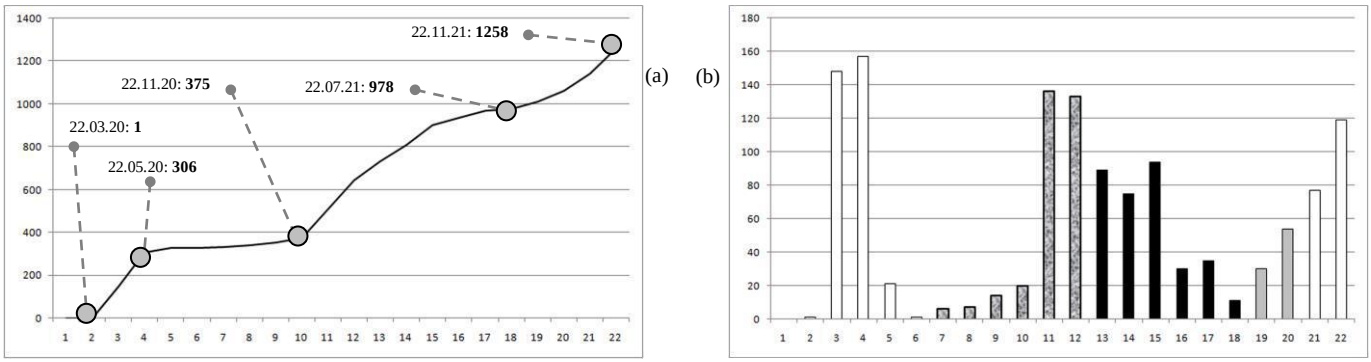
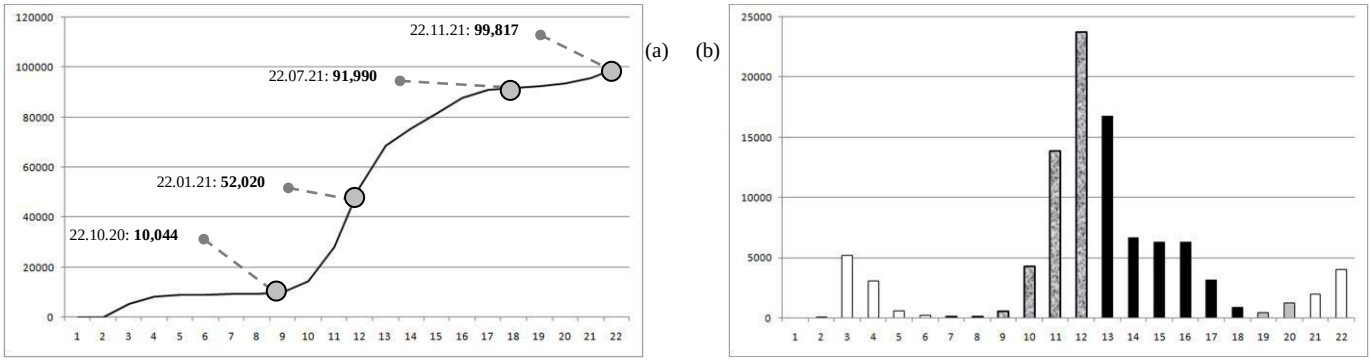
Finland



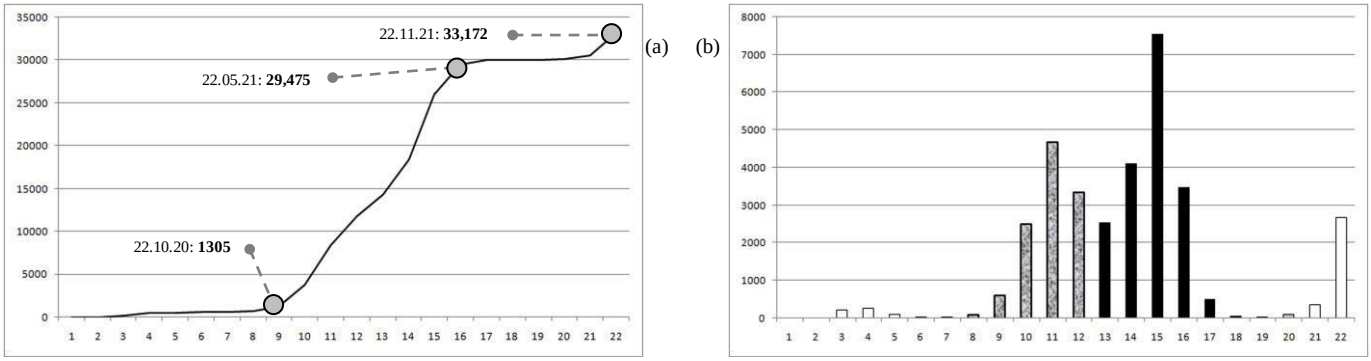
a) Dynamics of cumulative number of deaths in Finland a during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Finland.

Germany



a) Dynamics of cumulative number of deaths in Germany during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Germany.

Hungary



a) Dynamics of cumulative number of deaths in Hungary during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Hungary.

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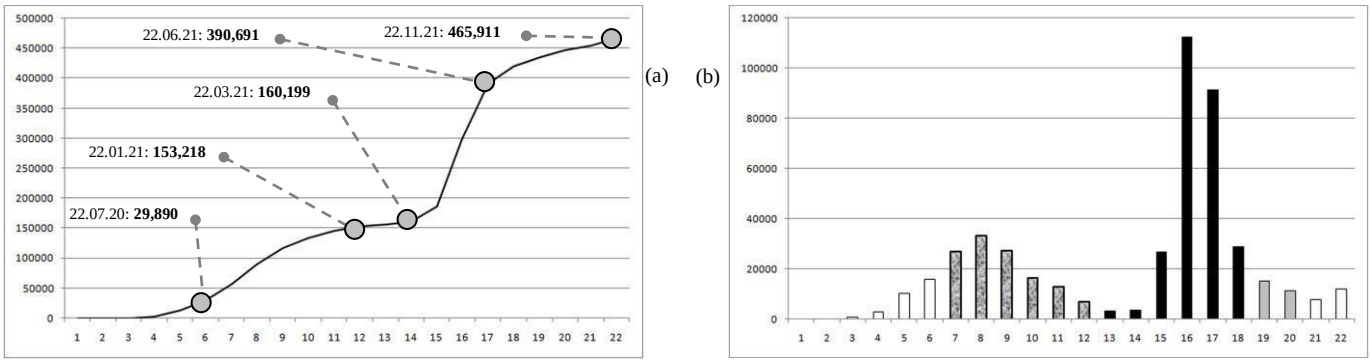
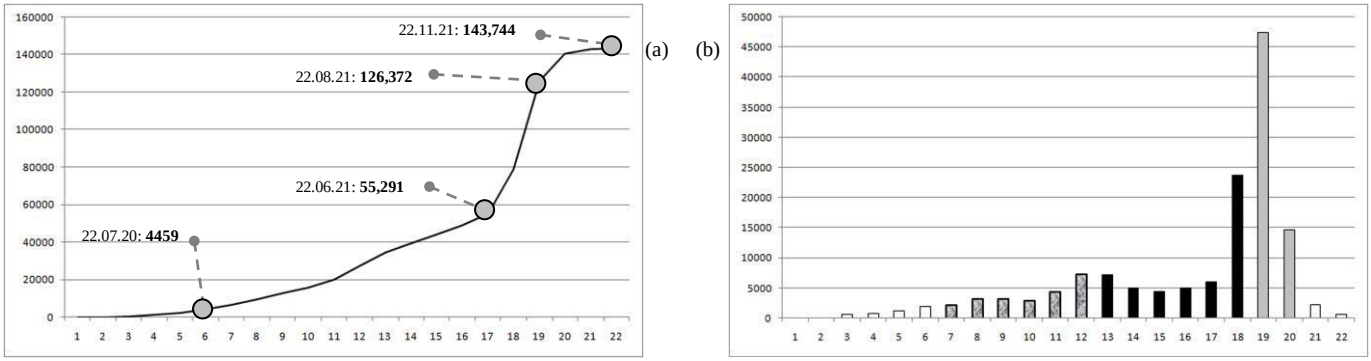
India



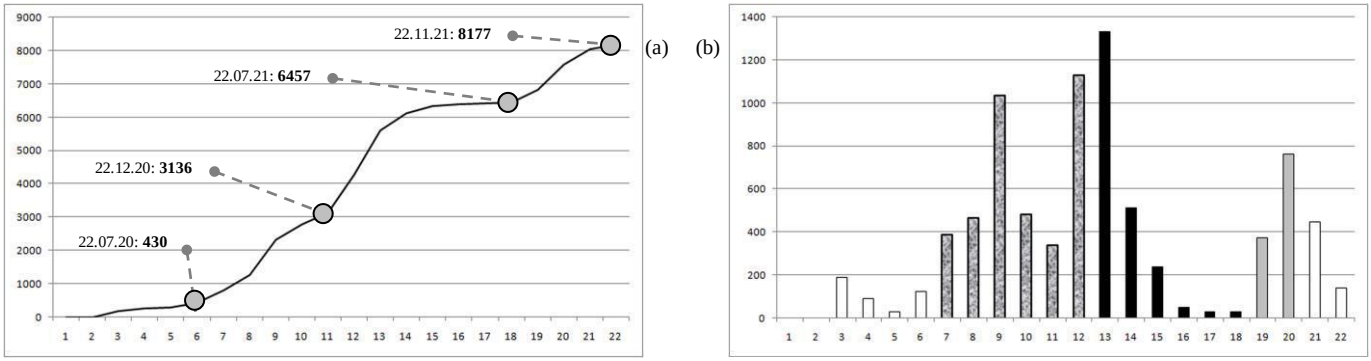
a) Dynamics of cumulative number of deaths in India during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in India.

Indonesia



a) Dynamics of cumulative number of deaths in Indonesia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Indonesia.

Israel



a) Dynamics of cumulative number of deaths in Israel during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Israel.

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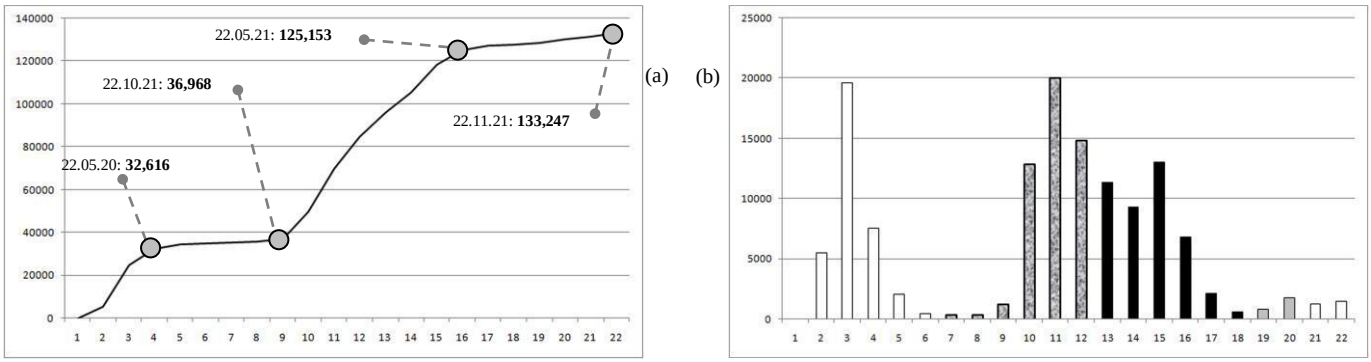
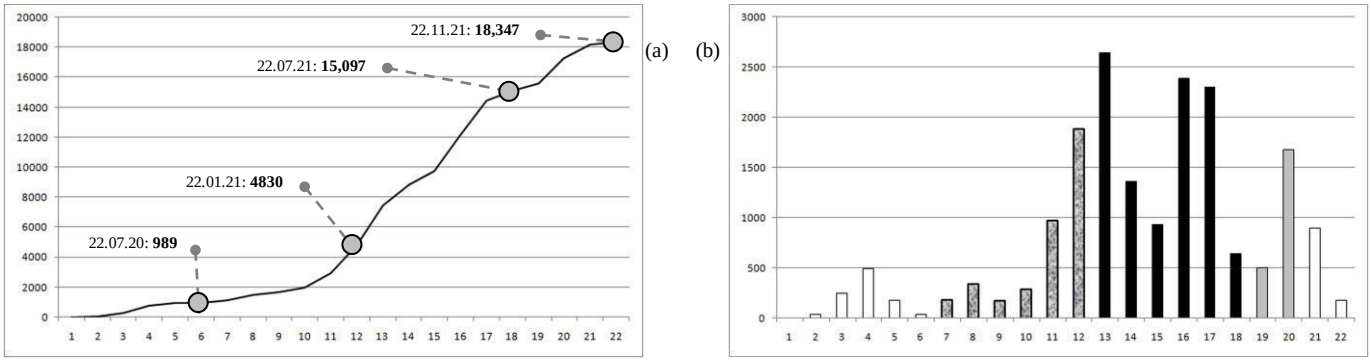
Italy



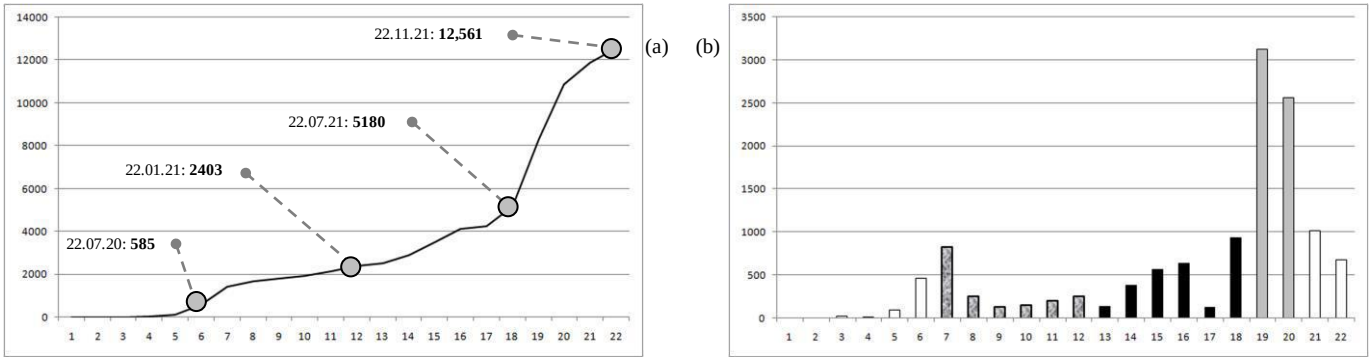
a) Dynamics of cumulative number of deaths in Italy during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Italy.

Japan



a) Dynamics of cumulative number of deaths in Japan during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Japan.

Kazakhstan



a) Dynamics of cumulative number of deaths in Kazakhstan during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Kazakhstan.

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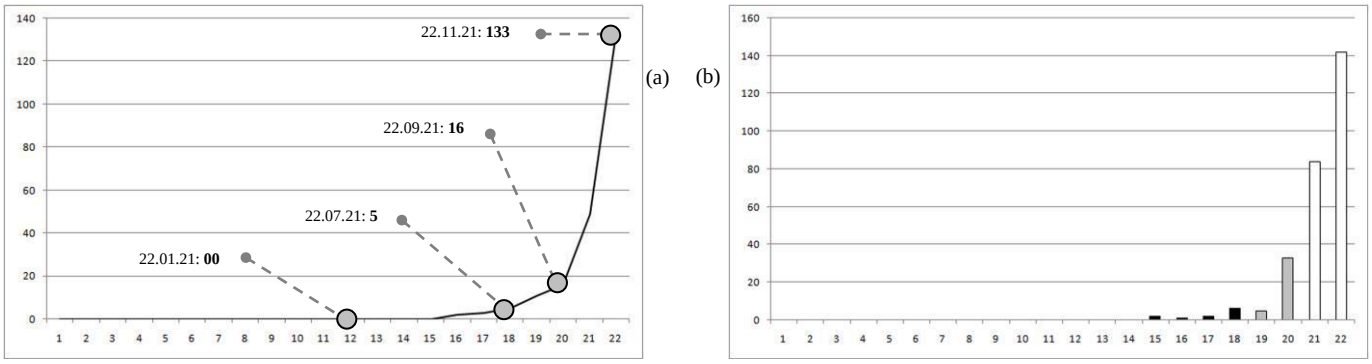
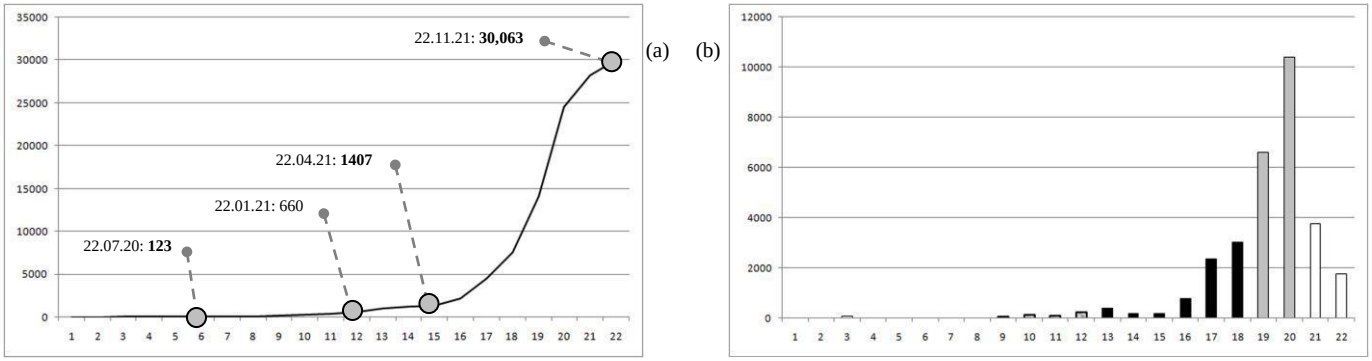
Laos



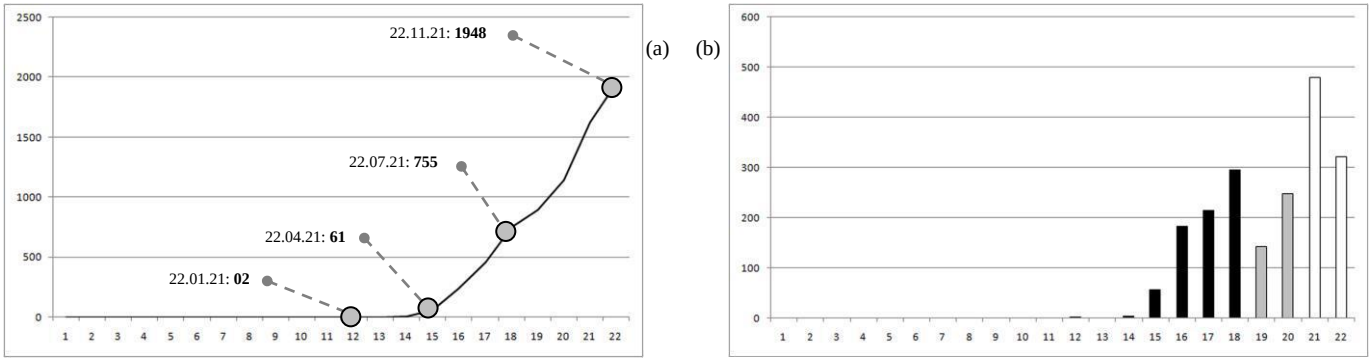
a) Dynamics of cumulative number of deaths in Laos during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Laos.

Malaysia



a) Dynamics of cumulative number of deaths in Malaysia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Malaysia.

Mongolia



a) Dynamics of cumulative number of deaths in Mongolia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Mongolia.

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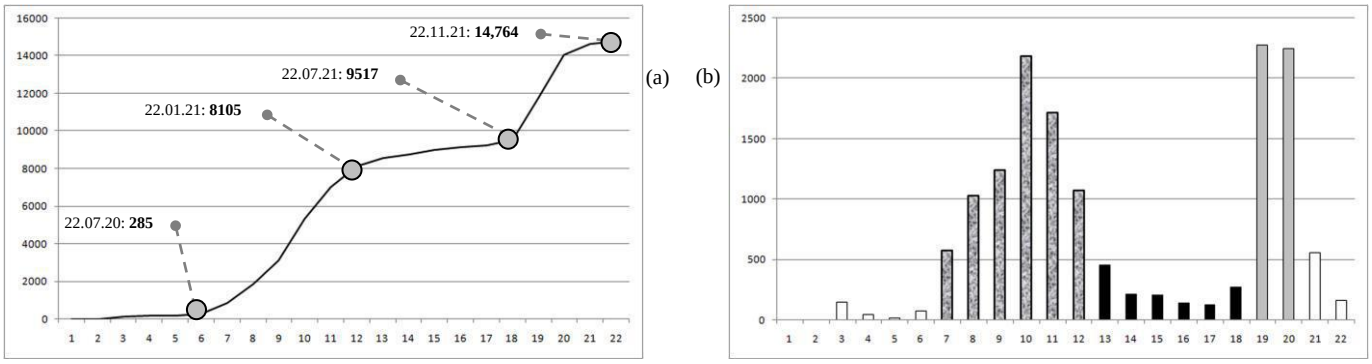
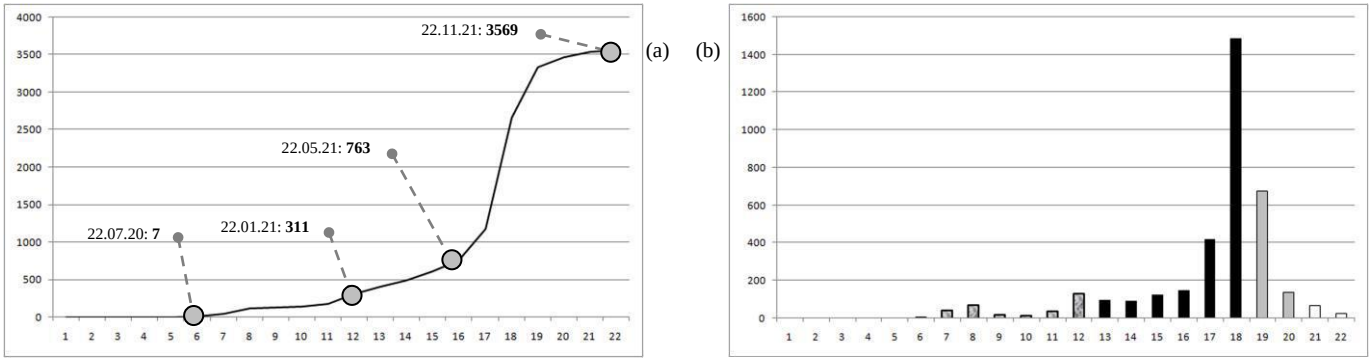
Morocco



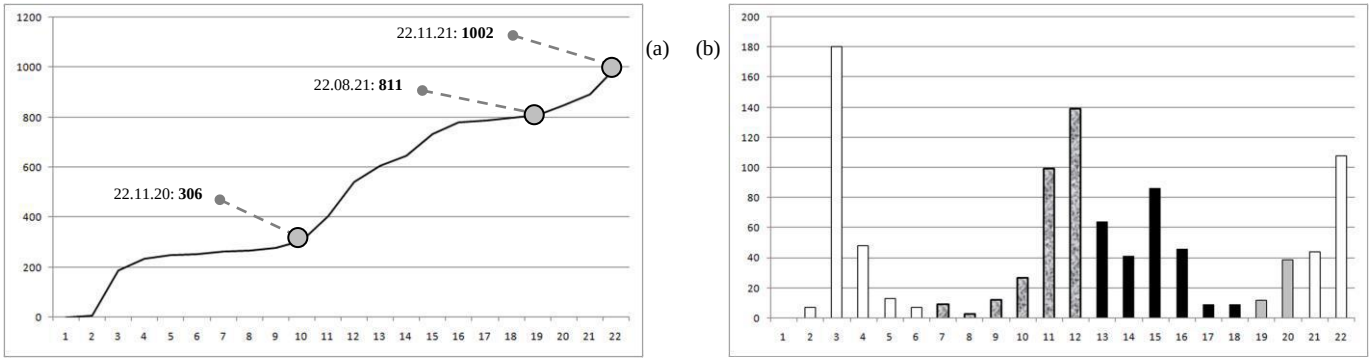
a) Dynamics of cumulative number of deaths in Morocco during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Morocco.

Namibia



a) Dynamics of cumulative number of deaths in Namibia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Namibia.

Norway



a) Dynamics of cumulative number of deaths in Norway during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Norway.

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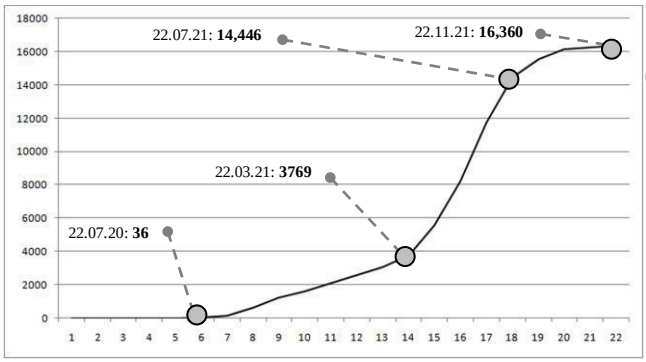
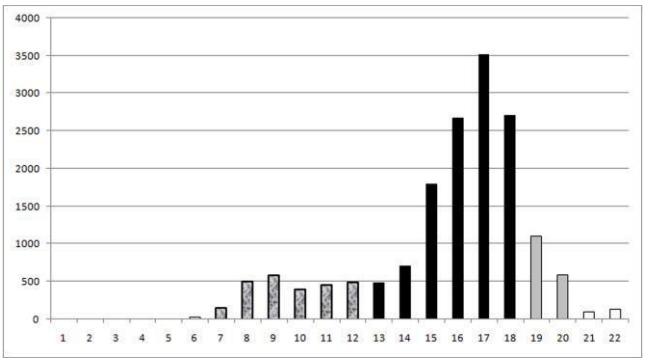
Paraguay

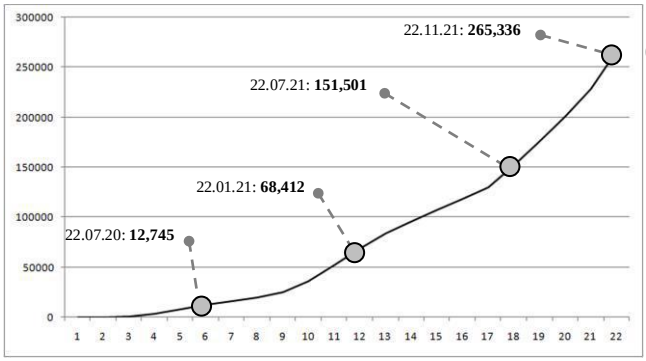


(a) (b)



a) Dynamics of cumulative number of deaths in Paraguay during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Paraguay.

Russia



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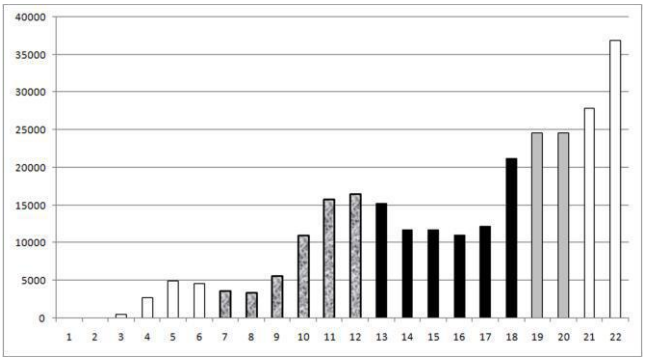
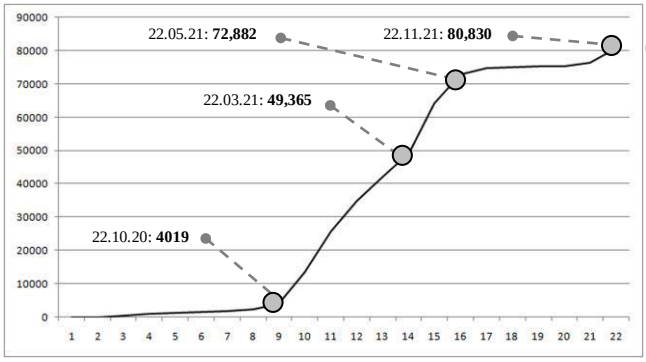


a) Dynamics of cumulative number of deaths in Russia during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Russia.

Poland



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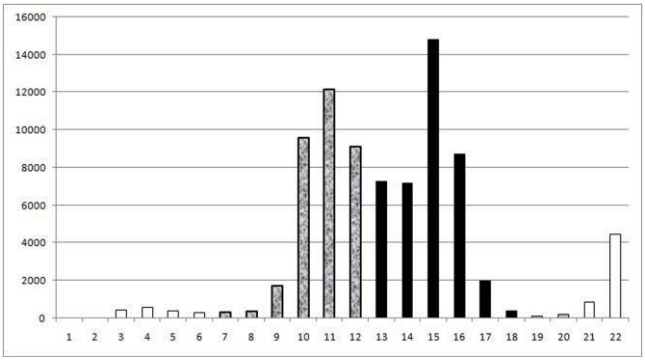

a) Dynamics of cumulative number of deaths in Poland during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Poland.

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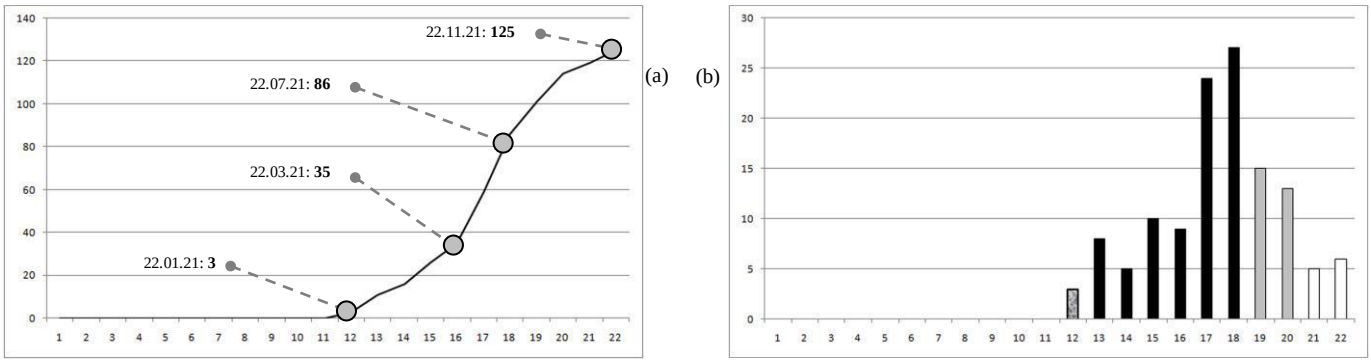
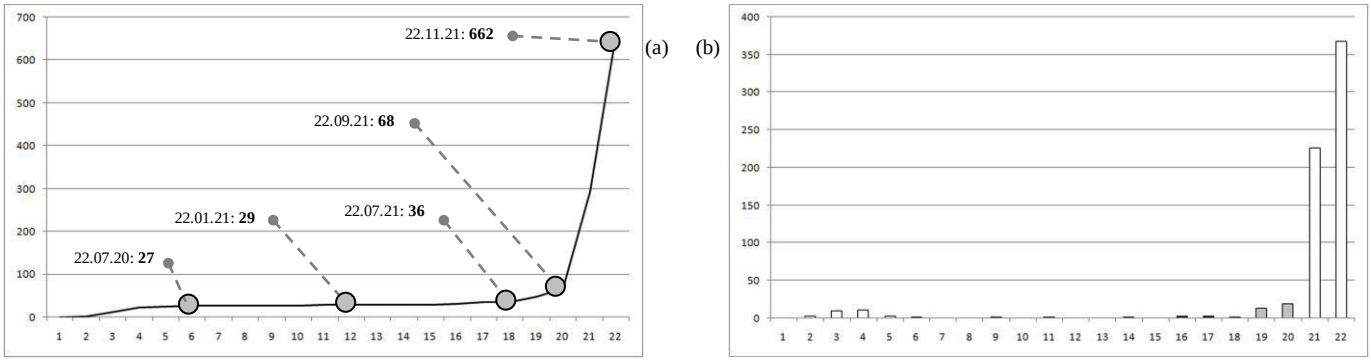
The Seychelles



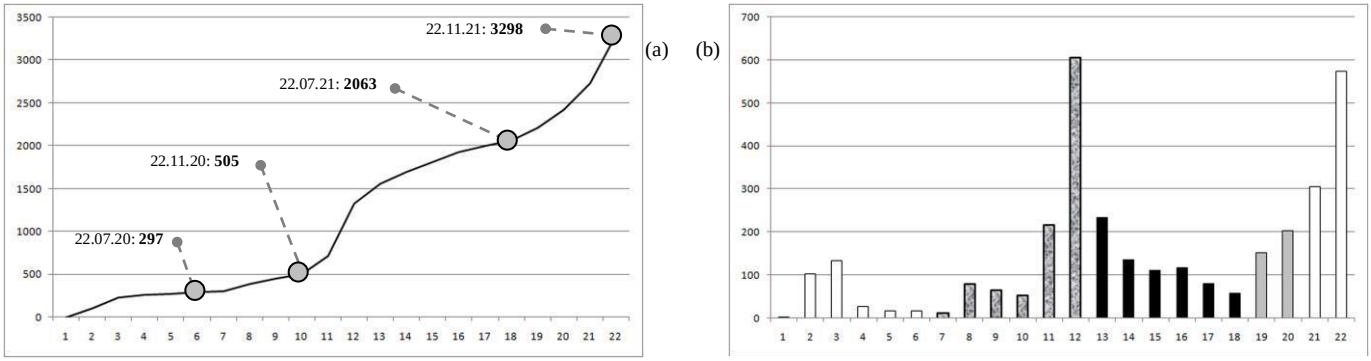
a) Dynamics of cumulative number of deaths in The Seychelles during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in The Seychelles.

Singapore



a) Dynamics of cumulative number of deaths in Singapore during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Singapore.

South Korea



a) Dynamics of cumulative number of deaths in S. Korea during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in S. Korea.

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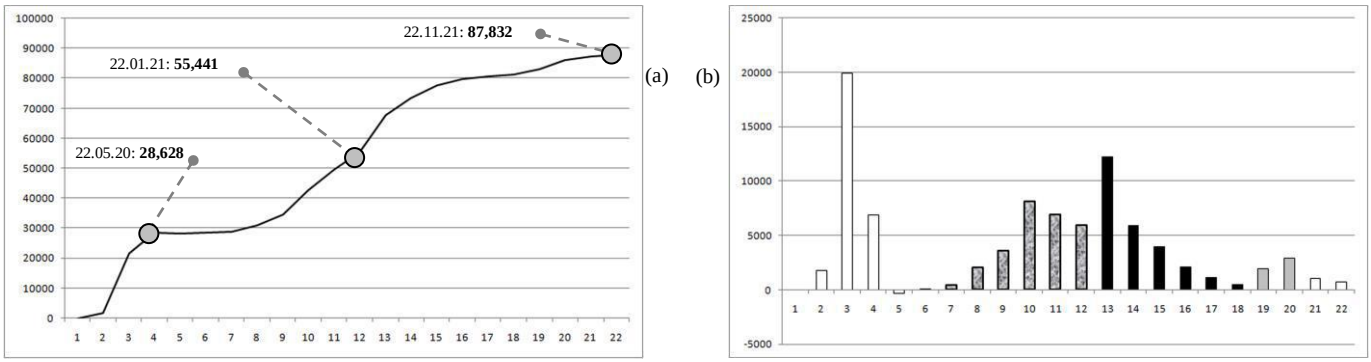
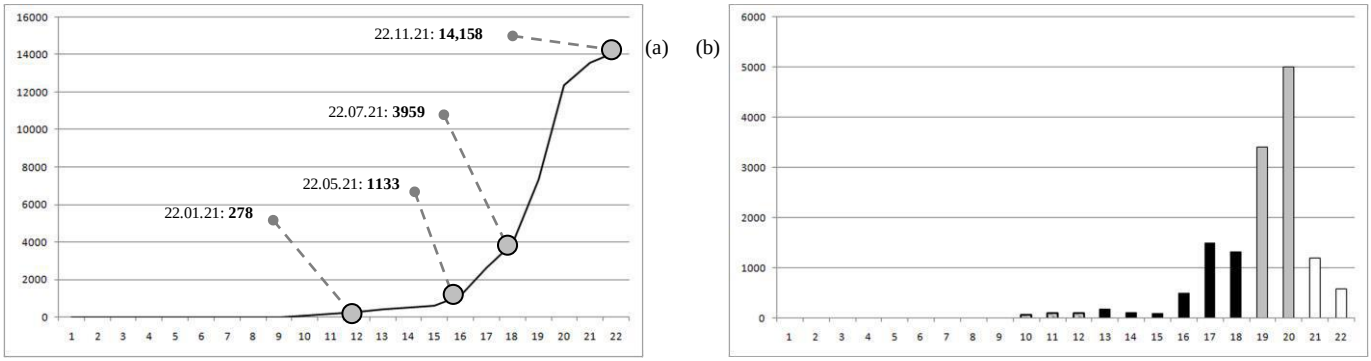
Spain



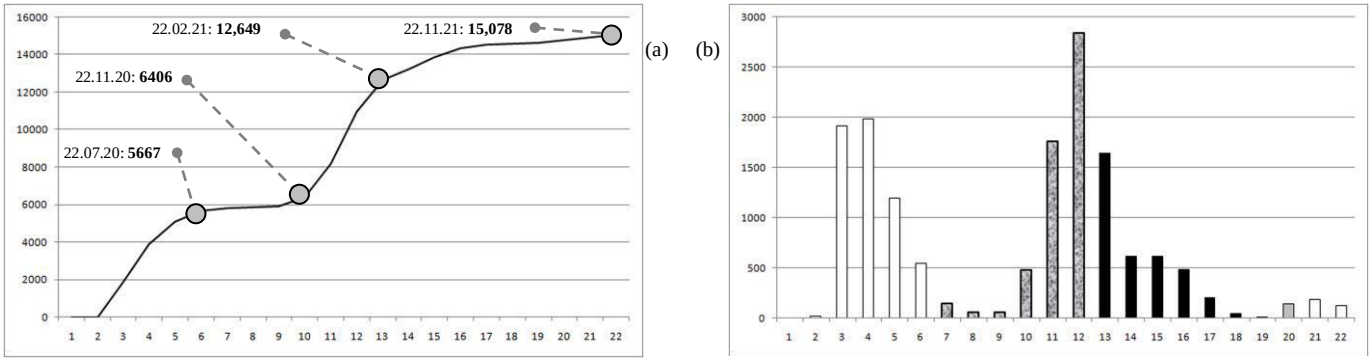
a) Dynamics of cumulative number of deaths in Spain during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Spain.

Sri Lanka



a) Dynamics of cumulative number of deaths in Sri Lanka during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Sri Lanka.

Sweden



a) Dynamics of cumulative number of deaths in Sweden during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Sweden.

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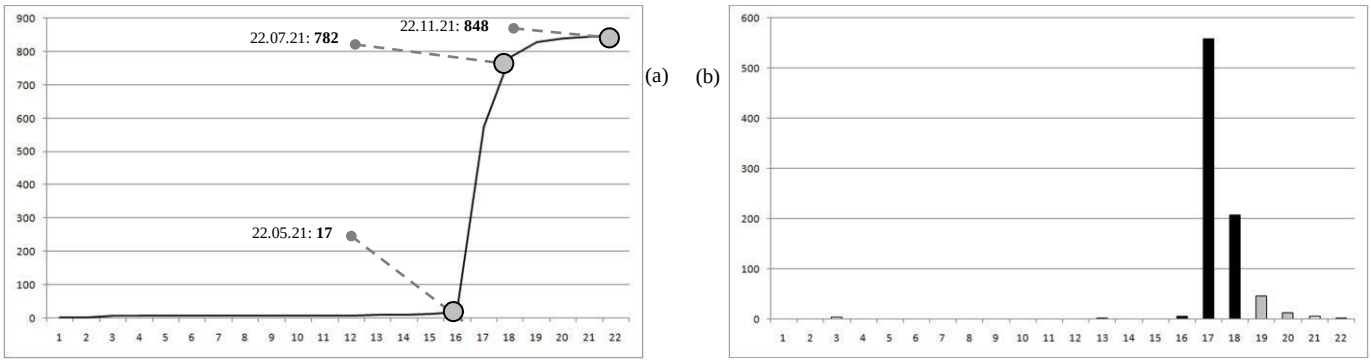
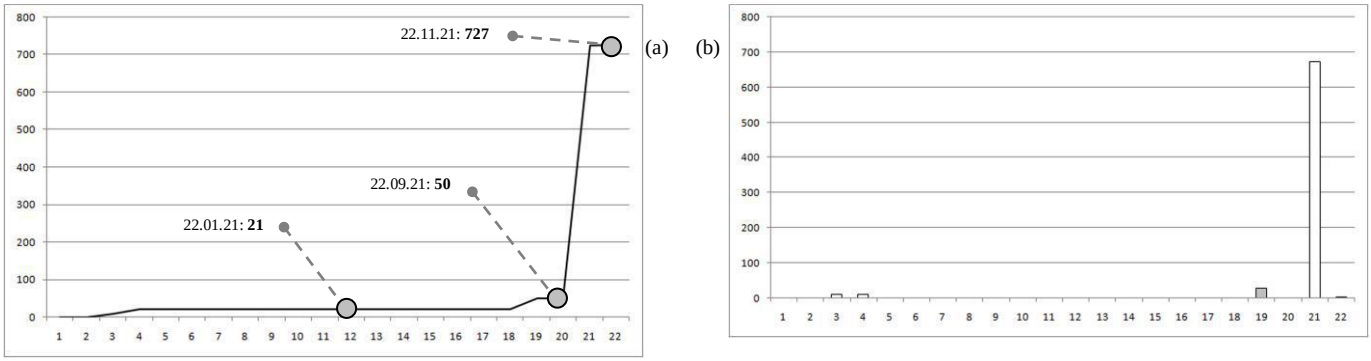
Taiwan



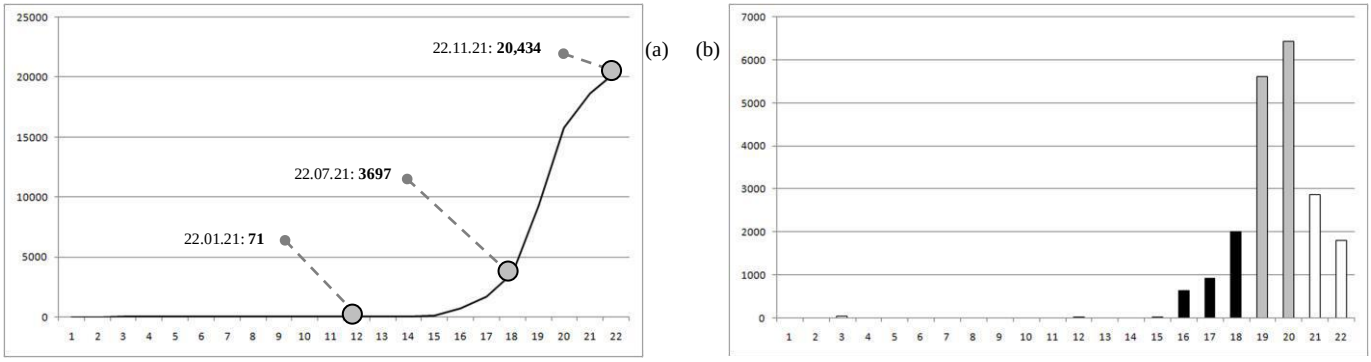
a) Dynamics of cumulative number of deaths in Taiwan during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Taiwan.

Tanzania



a) Dynamics of cumulative number of deaths in Tanzania during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Tanzania.

Thailand



a) Dynamics of cumulative number of deaths in Thailand during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Thailand.

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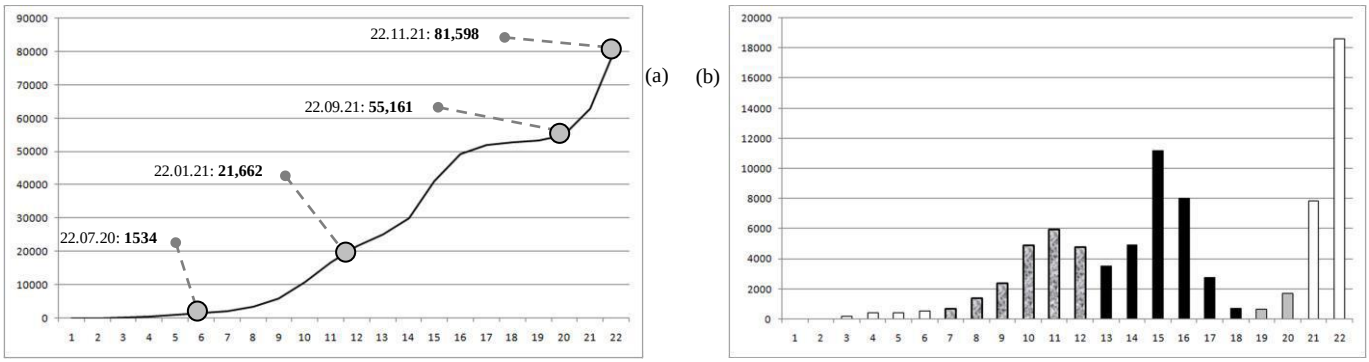
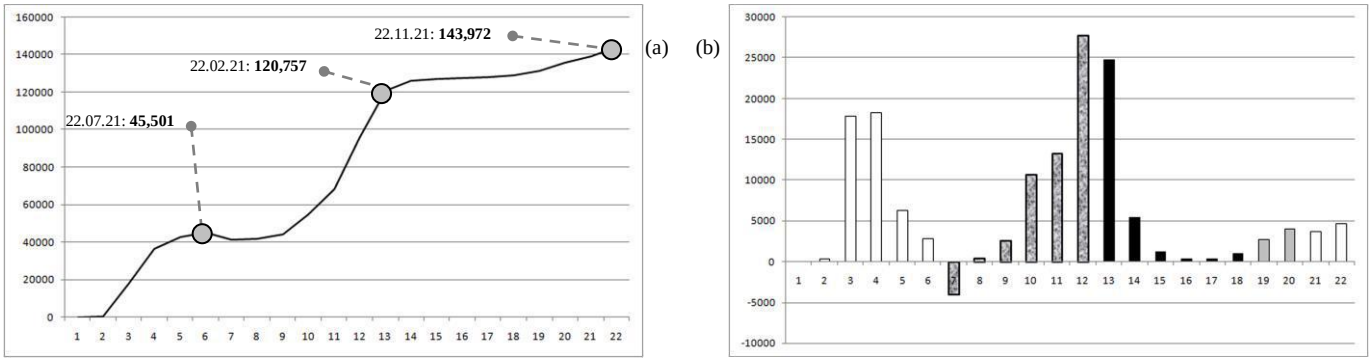
Ukraine



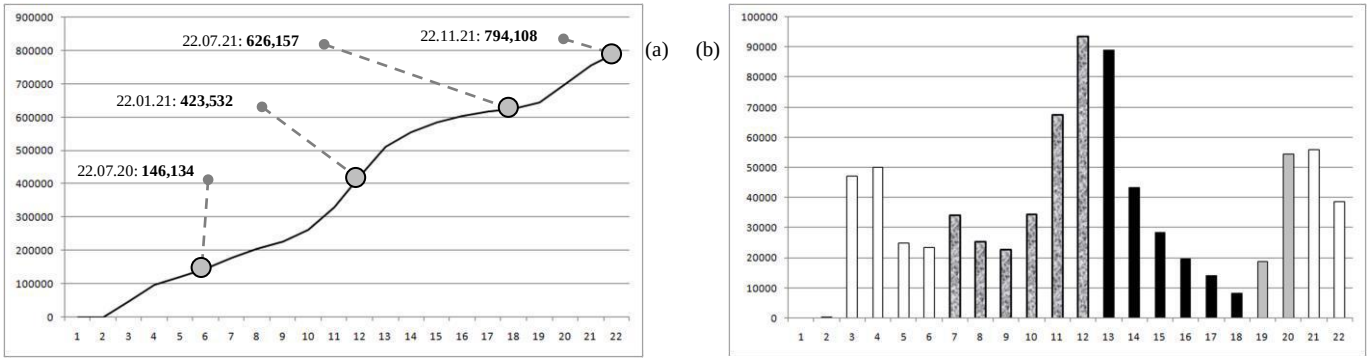
a) Dynamics of cumulative number of deaths in Ukraine during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Ukraine.

The United Kingdom



a) Dynamics of cumulative number of deaths in The United Kingdom during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in The United Kingdom.

The United States



a) Dynamics of cumulative number of deaths in The United States during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in The United States.

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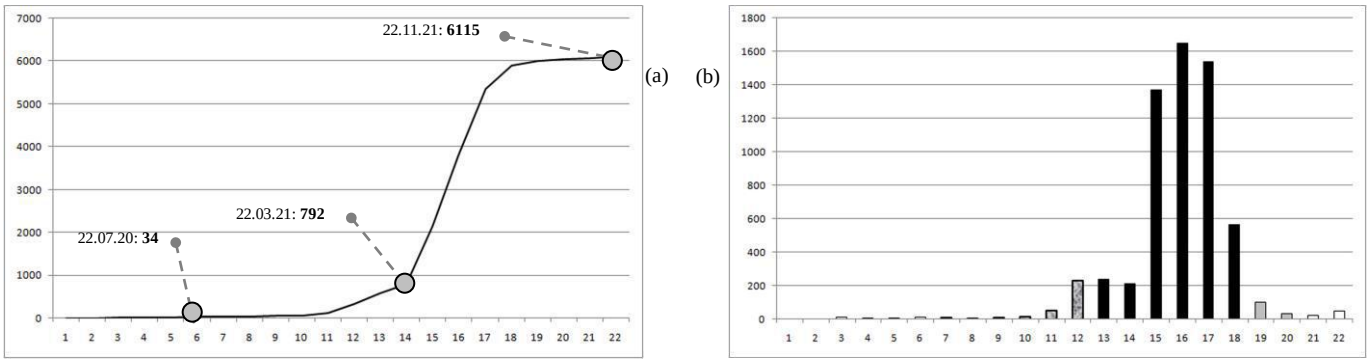
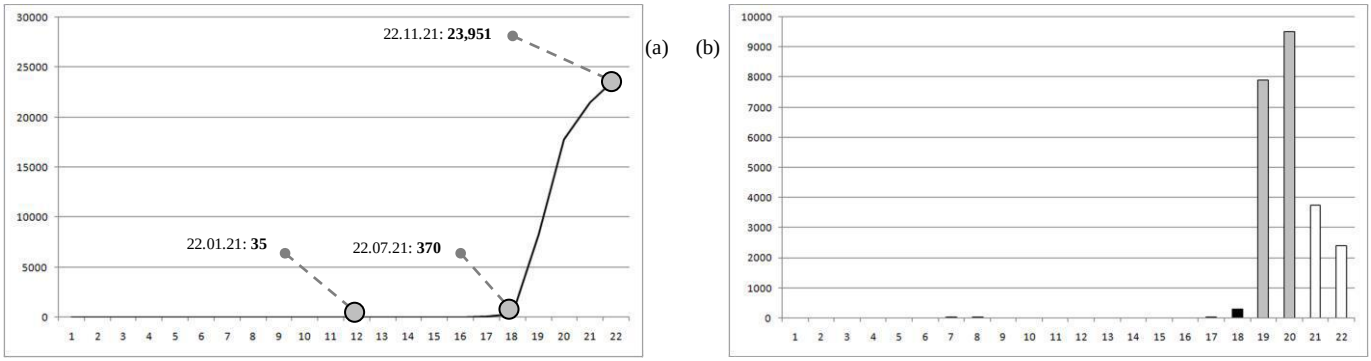
Uruguay



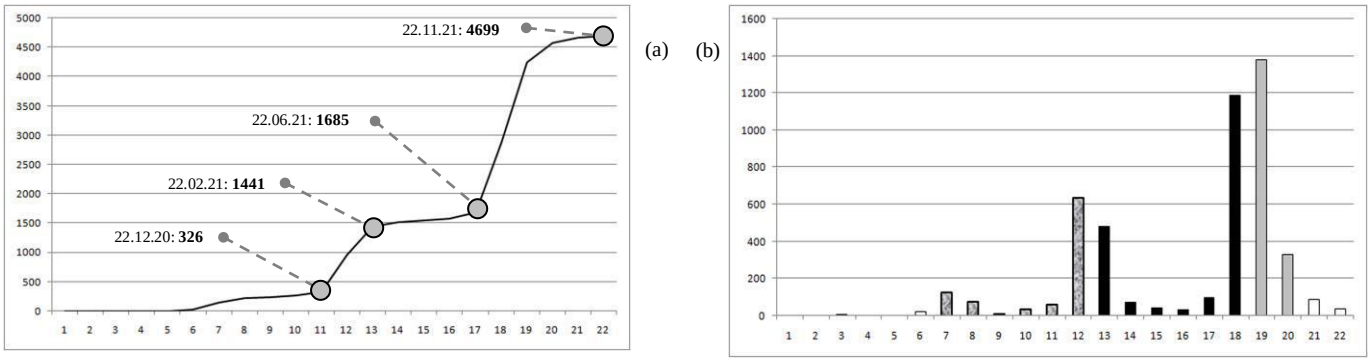
a) Dynamics of cumulative number of deaths in Uruguay during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Uruguay.

Vietnam



a) Dynamics of cumulative number of deaths in Vietnam during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Vietnam.

Zimbabwe



a) Dynamics of cumulative number of deaths in Zimbabwe during 22 months of the COVID-19 pandemic
b) Monthly number of deaths due to COVID-19 during the pandemic in Zimbabwe.